

PRIMARY HEADACHE

Headache-introduction

00:02:46

Pain sensitive cranial structures

Dura

Circle of Willis

Scalp

proximal segments of pial arteries

middle meningeal artery v, ix, x

Falx cerebri

Ependyma

Choroid Plexus

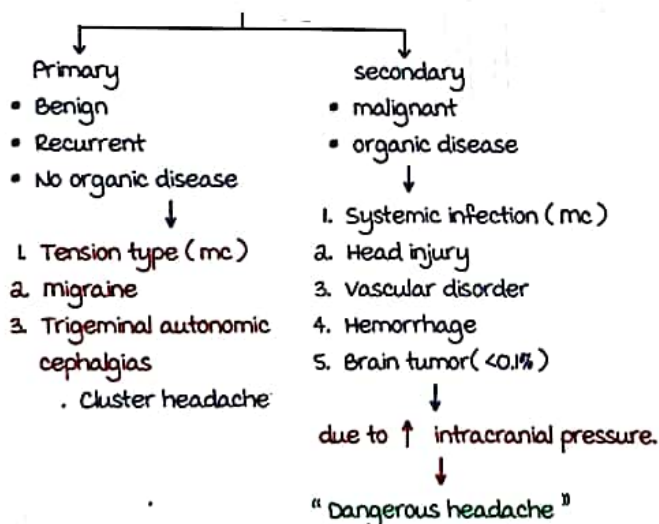
Pial veins

Brain parenchyma

} pain insensitive structures.

Headache classification

00:06:23



Tension headache

00:11:17

mc type primary headache

female >>> male (middle aged female)

30-45 years

One third of cases associated with depression

fullness or tightness or pressure band

↓
doesn't affect activities of daily living

Active space

Headaches

Sinus: pain is usually behind the forehead and/or cheekbones	Cluster: pain is in and around one eye	Tension: pain is like a band squeezing the head	Migraine: pain, nausea and visual changes are typical of classic form

No { vomiting
Photophobia
Phonophobia

Patient is never disturbed from sleep due to headache

Fundus → No papilloedema (↑ ICT)

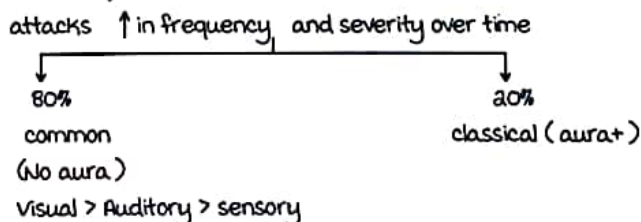
Treatment

1. Acute attack - NSAIDS
2. Chronic TTH - prophylaxis with Amitryptiline (TCA)

Migraine

00:17:34

- Episodic headache
- Started during school (10-15yrs)



- Zigzag lines MC
- Fortification spectra
- Scintillating scotomas

2 days prior to attack

↓

mood changes
irritability
Depression

Active space

Migraine headache features

00:22:37

Aura → visual (20-30 minutes)

↓ auditory, sensory.

Typical headache

U/L (sometimes become holocranial)

Site - Frontotemporal > orbital

Nature - Throbbing / pounding

Nausea + or - vomiting

4-72hrs per episode

photophobia / phonophobia / osmophobia

Aggravated by movement

After headache patient feels lethargic, depressed

O/E - normal

Repeated attacks of headache lasting 4-72 h in patients with a normal physical examination, no other reasonable cause for the headache, and:

At Least 2 of the Following Features:

Unilateral pain

Throbbing pain

Aggravation by movement

Moderate or severe intensity

Plus at Least 1 of the Following Features:

Nausea/vomiting

Photophobia and phonophobia

Migraine theories

00:31:28

Vascular theory

Blood vessel dilation

Vasoconstriction - "aura"

Vasodilation - "headache"

Triggers

- Glare
- Bright lights
- Sounds
- Hunger
- Excess stress
- Hormonal fluctuations during menses
- lack of or excess sleep
- Alcohol
- (or other chemical stimulation)

Pathology - CGRP (calcitonin gene related peptide)

Centre - Trigemino vascular complex

Rare types of migraine

00:35:06

1. Ophthalmoplegic migraine - transient U/L 3rd N Palsy



Completely reversible

2. Basilar migraine - Transient posterior circulation symptoms
ataxia/tinnitus/diplopia/vertigo
 3. Hemiplegic migraine - Transient weakness on one side
 4. Retinal migraine - Transient monocular visual loss
- Familial hemiplegic migraine - Ca^{2+} channelopathy

Episodic disabling headache of > 6 months duration with normal neurological examination is migraine until proven otherwise

Acute migraine Management

00:38:27

mild

Paracetamol

or

NSAIDS

-Naproxen 550 mg bd

-Ibuprofen 200 - 400 mg Q 4h

+

Antiemetics

Severe attack - 6mg s/c sumatriptan

Other drugs.

1) Ergot alkaloids - Dihydroergotamines

Issues with triptans

1. Triptan ineffective in classical migraine

2. CAD/CVA patient contraindicated

3. Clinical efficacy depends on T max

4. Headache recurrence is least for Ergotamines.

Newer treatment modality

- monoclonal Antibody against CGRP



Erenumab

moderate - Severe

- Triptans

- 5HT 1B/1D agonists

- Oral [Rizatriptan 5mg - 30mg
Eletriptan

40mg - 80 mg

sumatriptan (oral, nasal, sc)

Zolmitriptan (oral or nasal)

Prophylaxis of migraine

00:45:35

- First line - Propranolol
 TCA - Amitriptyline
 Topiramate
- Second line - Telmisartan
 Venlafaxine
 Valproate
- Third line - Pizotifen (5HT_{2c} antagonist)
 Flunarizine (CCB)
 Clonidine

Other modalities of treatment

1. Greater Occipital nerve block
 2. Onabotulinum toxin A
 3. supraorbital transcutaneous stimulation
 4. CGRP antagonists
- Differential diagnosis - sinusitis

Trigeminal autonomic Cephalgia

00:51:55

1. Clusters headache (mc)
2. Paroxysmal hemicrania
3. SUNCT
 (Short lasting unilateral neuralgic headache with conjunctival congestion & tearing)
4. Hemicrania continua

TACS: Episodic

1. u/L severe headache (sharp stabbing)
 2. Restlessness during attack
 3. Ipsilateral autonomic symptoms
- Episode : 15 mins - 3 hours

TAC-autonomic features

00:56:49

1. Cluster headache, congestion & lacrimation
2. Nasal congestion & rhinorrhoea
3. Eyelid edema
4. Forehead or facial sweating
5. Fullness in ear
6. Flushing
7. Ptosis /miosis

Cluster headache

1. Episodic, short lasting, U/L, severe
2. Autonomic symptoms
3. Restlessness

Cardinal points

- a. periorbital
- b. 15 mins - 3hrs, 1-8 attacks / day
- c. 8-10 weeks $\longrightarrow$ symptom free interval
of symptoms
- d. Stabbing or boring pain
- e. Nocturnal pain
- f. Precipitated by alcohol
- g. Photophobia $\pm$ (U/L)
- h. Young male

Features

- aka suicide headache

[20% Chronic
80% Episodic

Treatment of cluster headache

01:02:29

Treat 100% O₂ $\rightarrow$ 10 L/min for 10-15 mins
or
6mg s/c Sumatriptan

Short term $\leftarrow$ prophylaxis $\rightarrow$ Long term
Prevention
Steroids
Verapamil or
Lithium

Paroxysmal hemicrania

1) Episodic short lasting U/L headache (Severe)

2) Restlessness

3) Autonomic symptoms

Cardinal features

1. m=F, middle aged
2. Stabbing / boring periorbital pain
3. 5-20 attacks / day



Each attack 2-30 mins (5 min: average)

4. No nocturnal preponderance
 5. Rapid response to Indomethacin
 6. Periodicity not so striking
- Alcohol trigger : no

SUNCT

01:07:59

- Conjunctival congestion & tearing
 - Female > male
 - ↑ number of attacks
 - Each attack lasts for seconds
 - Cutaneous trigger - no refractory periods
 - Acute attacks → IV Lignocaine
 - Prevention → Lamotrigine
 - No migrainous features
 - Alcohol trigger: yes
- Hemicrania continua
- Elderly females
 - Continuous, U/L, migrainous features
 - Autonomic ++
 - Responsive to indomethacin
- IOC - MRI

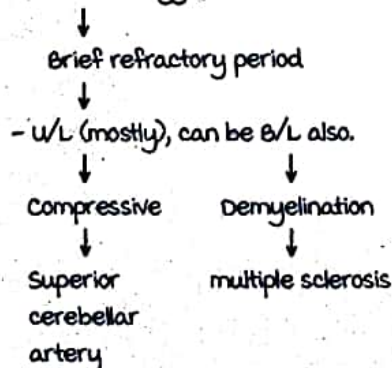
Trigeminal neuralgia

01:12:30

- Paroxysms of intense, brief, shock like superficial pain along the distribution of trigeminal nerve
- Few seconds to minutes
- Female > male
- 50 - 60yrs

Nature: V2/V3 (mc)
 usually ophthalmic division not involved
 ↓
 Objective neurological signs absent

Cutaneous trigger



Active space

Tic douloureux

Diagnosis - 3D MRI

DOC - Carbamazepine > Lamotrigine

S/ C botox



Refractory

microvascular decompression

HLA B - 1502 in carbamazepine causes SJS (Steven Johnson Syndrome)

Eagle's syndrome

- Enlarged styloid process.
- Glossopharyngeal neuralgia.

DANGEROUS HEADACHE

Secondary headache

00:00:25

- Dangerous headache → Increase Intracranial headahe .
- Cerebral Perfusion Pressure (CPP) = mean arterial pressure - Intracranial pressure
- Cerebral autoregulation .
- MAP → 50 - 150 mmHg → normal → CPP normal

Causes of Dangerous headache :

1. CNS infections
2. Vascular causes
3. Benign intracranial hypertension .
4. Brain tumors (space occupying lesions)
 - tumor , tuberculoma , neurocysticercosis .
5. Hemorrhage

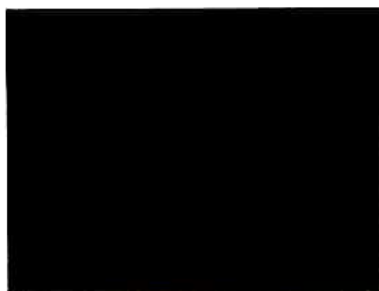
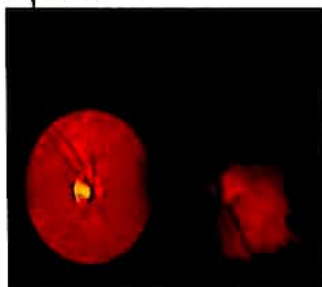
Features of dangerous headache

00:04:06

1. Sudden onset severe headache / time to peak
 - Bleed - ' Worst ever ' headache or ' thunder clap ' headache
2. Subacute onset headache → worsening in severity → associated with vomiting , bending , lifting or coughing
3. Disturbs sleep → early morning headache
4. Any new onset headache with visual blurring or tinnitus
5. Known systemic illness
6. Onset after age 55 → temporal arteritis
7. Fever or unexplained systemic signs .
8. Abnormal neurologic examination
9. Pain associated with local tenderness
 - eg → region of temporal artery .

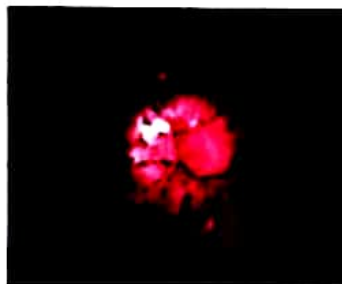
Investigations :

- Fundal examination → confirms increased ICT .
- Papilledema



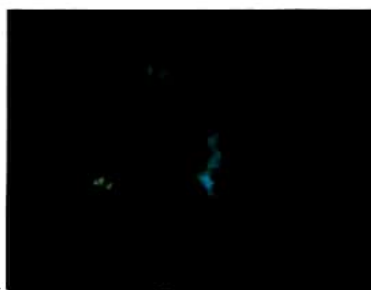
Active space

- Early papilledema diagnosed by presence of:
 - Peripapillary halo, with obscuration of borders, elevation of nasal border

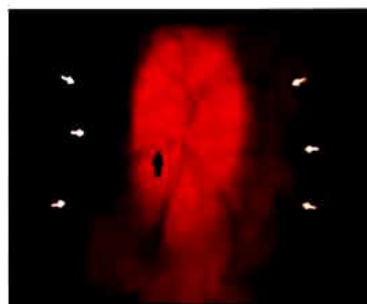


- marked papilledema
 - elevation of entire nerve head
 - obscuration of all the borders
 - projections
 - segment of major vessel obscured on the disc.

- Established papilledema
 - marked elevation of nerve head with blurring of margins.
 - engorged tortuous venules.
 - peripapillary splinter hemorrhages
 - Cotton wool spots.
 - hard exudates over the disc and macular area.



- Chronic papilledema
 - classical champagne cork appearance of disc.
 - Pale disc.
 - disc hyperemia decreases and disc progressively appears pale in color.
 - opticociliary shunts and drusen like deposits may be present on the disc.
 - high water mark.



Signs of raised intracranial tension

00:12:37

1. Cushing's reflex → bradycardia, bradypnea, hypertension.
2. Increased risk for arrhythmias.

- MRI Brain → to rule out intracranial space occupying lesions.

Brain herniation →

1. Cingulate herniation (Subfalcine)
2. Central transtentorial herniation

3. Uncal herniation (m.c)
4. Tonsillar herniation.

Cingulate herniation (subfalcine)

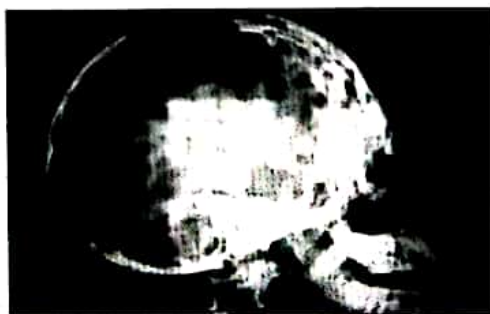
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1. Cingulate gyrus
2. Anterior cerebellar artery (ACA)
3. Internal cerebral vein



Uncal Herniation :

- third nerve palsy
- PCA occlusion
- Kernohans notch :
 - weakness on the side of herniation , called as ipsilateral hemiplegia
- hemiplegia false localizing sign → Pressure ischaemia
- third cranial nerve palsy
- PCA occlusion .
 - as the herniating temporal lobe pushes the midbrain towards the opposite side of the inscure
- contralateral cerebral peduncle is forced against the hard edge of the tentorium .
- Abducent nerve palsy → false localizing sign (m.c)
 - sign of Raised ICP
- X- ray finding of Increased ICP :- silver beaten appearance .



Active space



- a → subfacial (cingulate) herniation
- b → uncal herniation
- c → downward (Central, transtentorial) herniation.
- d → external herniation (not used now)
- e → tonsillar herniation.

Cases

00:24:12

Dangerous headache ± blurring of vision in a healthy individual,
Fundus → papilledema
MRI → normal (no intracranial space occupying lesion) → Sixth nerve palsy.

CASE I

1. Cerebral venous thrombosis (CVT)

- headache + vomiting + signs of increased ICP, non specific weakness.
- Infarcts with secondary hemorrhagic transformation.
- MRI is required (specially in post partum) IOC.
- CVT more common in post partum, females, underlying coagulopathies.

CT findings in CVT

- Cord sign → hyperdensity along the lines of transverse sinus.
- Dense triangle sign (Delta sign)
- Empty delta sign → in contrast enhanced CT.

- MR venography is the investigation of choice.
- Empty delta sign

CASE II

2. Benign intracranial hypertension (Pseudotumor cerebri)

- LP opening pressure more than 25 cm of H₂O
- 30 - 40 years, obese females.
- symptoms → headache, blurring of vision, tinnitus.
- fundus → Papilledema

MRI → No mass.

MRV → Normal

MRI shows → Empty sella → primary empty sella syndrome.



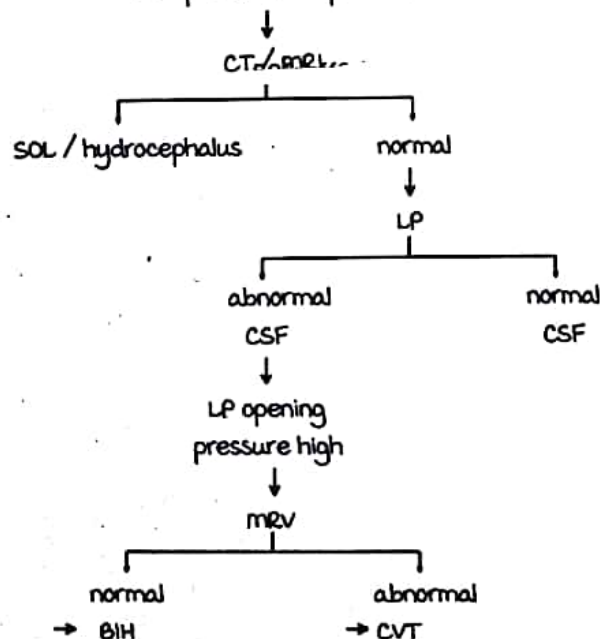
Modified dandy criteria

00:36:00

1. symptoms of raised ICP (headache, nausea, vomiting, transient visual obscuration, or papilledema)
2. no localizing signs with the exception of 6th nerve palsy patient is awake and alert.
3. normal CT/MRI findings without evidence of thrombosis.
4. LP opening pressure of more than 25 cm H₂O and normal biochemical and cytological composition of CSF.
5. no other explanation for the raised ICP

Approach:

Papilledema in a conscious alert patient with no neurologic signs except 6th nerve paresis



secondary causes of benign intracranial hypertension

1. Electrolyte abnormality → Hypocalcemia
2. Lead poisoning
3. Drugs : • Growth hormone / Steroids / Danazol
 - Outdated tetracyclines .
 - Nitrofurantoin
 - Vitamin A
 - Lithium

Treatment of BIH :

→ Weight loss

→ Acetazolamide
or
Topiramate] 1-4g / day (D.O.C)

+

Furosemide

→ Repeated LP → Symptom relief

→ Refractory cases → CSF shunting

or

Optic nerve sheath fenestrations

management of acute increased ICP :

1. Elevate head end .
 2. mannitol (15 to 30 mts for action)
 3. Sedation
 4. Hyperventilation
 5. Pressor therapy to maintain CPP > 60 mmHg .
- Thunderclap headache → most important cause sub arachnoid hemorrhage

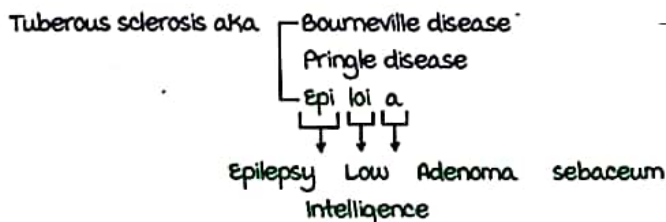
Other causes of thunder clap headache are

1. Apoplexy (Pituitary)
 2. Acute hydrocephalus
 3. CVT
 4. Dissection (carotid or vertebral)
 5. Hypertensive crisis (ICH, HTN encephalopathy)
- CT sign → star of death

NEUROCUTANEOUS SYNDROMES

- A/K/A Neurooculocutaneous syndromes (embryonic ectoderm)
- A/K/A Phakomatosis

1. Neurofibromatosis MC
 - NF - 1 - von Recklinghausen (Peripheral)
 - NF - 2 - central disease
2. Tuberous sclerosis
3. Von Hippel Lindau disease
4. Sturge Weber syndrome
5. Ataxia telangiectasia



Sturge Weber syndrome (A/K/A Encephalotrigeminal angiomatosis)

Neurofibromatosis

00:04:00

MC Phakomatosis

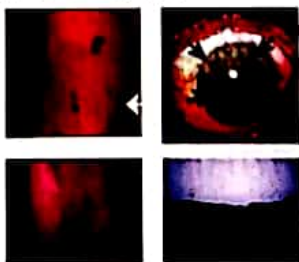
NF - 1 → Neurofibromin, autosomal dominant chromosome 17

Earliest manifestation - cafe au lait spots (within 1 year)

- Hyperpigmented; pre pubertal > 5mm

≥ 6 spots

- post pubertal > 15mm



Cafe au lait spots also seen in McCune Albright syndrome

- Neurofibromas

MC - Peripheral - Requires a lesions to make diagnosis

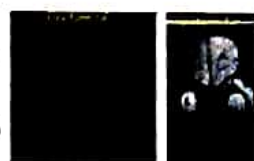
- Plexiform (even 1 single neurofibroma is sufficient)



Plexiform neurofibromas → premalignant

- Seen along the distribution of cranial nerves

- Cutaneous & subcutaneous neurofibroma
- Infraorbital and facial branches of CN III - VI
- Most commonly affects CN V
- Diffuse plexiform neurofibroma of face and eyelid



Axillary freckles - Specific

- Small (0.5 cm) brown, well circumscribed macules
- Rarely in inguinal region
- Generally unnoticed



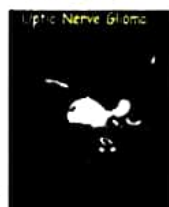
Optic nerve glioma: MC tumor seen in NF - I

- > 80 % are asymptomatic
- B / L optic nerve gliomas - Diagnostic

Features on CT

- Abnormal enhancement
- Abnormal thickening
- Beading and elongation.

Optic nerve glioma > Astrocytoma
> Brain stem glioma

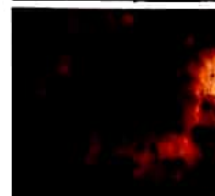
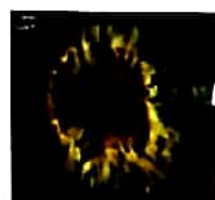


Other manifestations of NF - I

00:11:32

Lisch nodules - Iris

- A pigmented hamartomatous nevus affecting the iris
 - Benign nodule (do not affect vision)
 - No risk for malignancy
 - Adult onset finding
 - Only seen in slit lamp
- Diagnosis - 2 or more Lisch nodules



First degree relative in NF - I

Bone changes

MC - Kyphoscoliosis > cortical thinning of long bones

classical - sphenoid dysplasia

Neurofibromas - peripheral nerve sheath tumors

Other Features

1. Astrocytoma
2. Brainstem glioma
3. Meningioma
4. Hypertension
5. Mental impairment

Bony (less common)

1. Enlargement of intervertebral foramen
2. Ribbon ribs - Hypertrophied and twisted ribs
3. Posterior intervertebral scalloping

Neurofibromatosis - II

00:18:02

- Central neurofibromatosis
- B / L acoustic neuroma (Vestibular Schwannoma)
- U / L acoustic neuroma

+	or	+ 2 / 5
First degree relative		1. Neurofibroma 2. Meningioma 3. Schwannoma 4. Glioma 5. Posterior subcapsular cataract

Schwannomin / merlin gene - Chr. 22

Cutaneous manifestations are rare.

Other tumors - spinal cord ependymoma

- Commonest presentation of vestibular schwannoma is progressive high frequency SNHL
- Meningiomas < 20yrs, benign
- Spinal cord tumors : Schwannoma > Ependymoma (mc)
- Schwannomas with NF-2 never undergo malignant change
- No cognitive impairment / MR
- No hypertension

Tuberous sclerosis

00:23:44

- AD with variable expression
- Spontaneous mutation

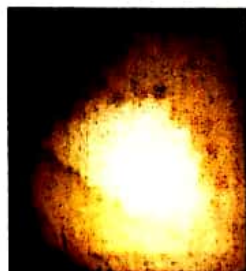
TSC ₁	chr. 9	Hamartin
TSC ₂	chr. 16	Tuberin

 (poor prognosis)

manifestations :

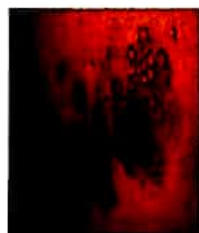
I Ashleaf macule

Earliest manifestation - hypopigmented



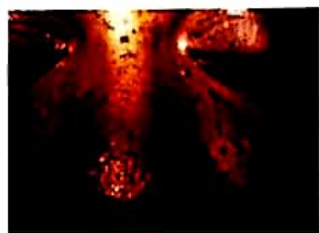
II Shagreen patch

- 1 - 2 yrs age
- Lumbosacral region / buttocks



III Adenoma sebaceum

- Cutaneous angiofibromas



IV Fibrous plaques on forehead - specific

CNS manifestations

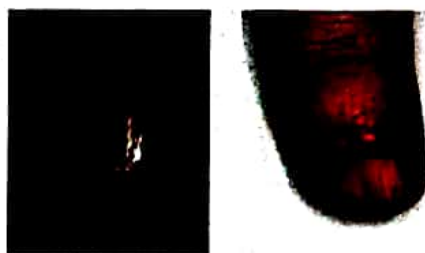
1. Earliest commonest] Cortical tubers → seizure (Epileptical hamartomas)
2. 2nd MC : subependymal nodules
3. Subependymal giant cell astrocytoma (MC tumor)
↓
(SEGCA)
Obstructive Hydrocephalus
4. Infantile spasms
5. White matter lesions.



Parieto occipital



Groove of lateral ventricle



SEGA

Moen's tumor - Periungual fibroma (MC)
Subungual fibroma

Systemic wise manifestation of tuberous sclerosis

00:30:22

1. Heart
 - Cardiac rhabdomyoma
 - Prenatal diagnosis of rhabdomyoma



80 % risk for tuberous sclerosis

- Apex of LV (MC site)
- Benign tumor

2. Eyes

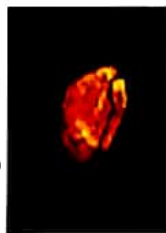
- Retinal hamartomas - don't affect vision
- Retinal achromic patch
- Retinal astrocytomas

3. Lung

- ↑ risk for ILD
- Pulmonary lymphangiomyomatosis
- F > M
- Cysts, pneumothorax
- Rarely premalignant

4. Kidney

- MC, Renal angiomyolipoma
- ↓
- bleeds into retroperitoneum
 - Bilateral large cyst
 - 1-2 % risk for RCC



5. Other

- Dental enamel pits - 100 % patients
- Confetti skin lesions - numerous hypopigmented macules over arms and legs.
- Bone cyst
- Hamartomatous rectal polyp
- Gingival fibroma

Active space

Von hippel lindau disease

00:36:45

- AD (chr. 3p)
- No cutaneous manifestations

Systemic manifestations

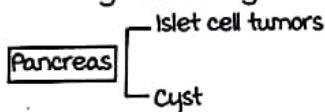
- C - Clear cell ca. of comma in between kidney and cysts in liver, kidney and pancreas
- H - Hemangioblastoma of cerebellum and retina
- I - Islet cell tumor of pancreas
- P - Pheochromocytoma, papillary cystadenoma of uterus
- E - Endolymphatic sac tumor comma b/w tumor and epididymal cyst
- S - Spinal cord tumors

Clear cell Ca

Non-VHL	VHL
Sporadic	AD
Elderly	Young
m > F	m = F
Smoker	Non smoker
U / L	B / L
Blood spread	Lymphatic spread

VHL - very few bilateral renal cysts

- RCC
- Cysts classically seen in pancreas



Hemangioblastoma - Cerebellar (mc)
Retinal
Spinal cord

Pheochromocytoma - malignant
- Often Bilateral

Hemangioblastoma :

- mc age : 20 - 50 years
- multiple
- Seen in 2/3 patients of VHL
- Hall mark lesion of VHL
- mc cerebellar > medulla > Pons > Spinal cord (CNS)
- Epo secreting tumor, → polycythemia
- Retinal - no visual loss

Renal :

- RCC
- Renal cysts - multiple, Bilateral

Pancreas :

- Cysts
- Islet cell tumor

Sturge weber syndrome

00:44:08

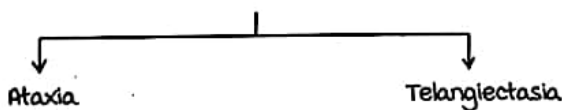
- Sporadic
- No brain tumor
- Aka encephalo trigeminal angiomatosis .
- 1) Port wine stain at birth (U/L)
- 2) Leptomeningeal capillary or venous malformation always ipsilateral
- 3) Cerebral hemiatrophy
- C/F
 - a. Seizures
 - b. Congenital glaucoma / buphthalmos .
 - c. MR

Calcification - Tram track / Rail track



Ataxia telangiectasia

00:48:33



- Autosomal recessive
 - AT gene (Chr 11)
 - Cerebellar ataxia (2 - 4 yrs)
 - Oculomotor apraxia (2 - 8 yrs)
 - Choreaathetosis
- } Triad

Oculocutaneous telangiectasia

- Friedreich's ataxia - spinocerebellar tract problem
- Ataxia telangiectasia - cerebellar atrophy



Friedreich's ataxia



Ataxia telangiectasia

1. Cutaneous granulomas
2. Defective DNA repair and ↑ risk for malignancy
3. Progeria (early onset aging)
4. Hypertrichosis

MC malignancy - ALL (T cell > B cell)

- Dysgerminoma > HCC > Ca. stomach > Retinoblastoma
- Increased risk of sinopulmonary infection

Diagnosis

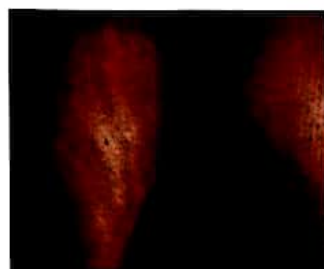
- α - Fetoprotein ↑
- Hypogammaglobulinemia (IgG ↓)
- Chromosomal breaks (14 chr)
- Cerebellar atrophy.

Rare neurocutaneous syndromes

00:53:42

I Hypomelanosis of ito

- 1) Sporadic
- 2) 3rd MC neurocutaneous syndrome
NF > TSC > Hypomelanosis of ito
- 3) Hypopigmented whorls, streaks and patches tend to follow Blaschko lines.



II Incontinentia pigmenti A/I/A Bloch-Sulzberger syndrome

- 1) X-linked dominant
- 2) Functional mosaicism
F > m
- 3) Blisters and verrucous lesions

III Phace syndrome

- P - post. fossa malformation
- H - Hemangioma
- A - Arterial anomalies
- C - Coarctation of aorta
- E - Eye anomalies

APPROACH TO PERIPHERAL NEUROPATHY

Lower motor neuron (LMN) Pathology:

1. lesions - lesion in ? distal to the anterior horn cell (AHC)

- lesion in ? distal to the cranial nerve nuclei

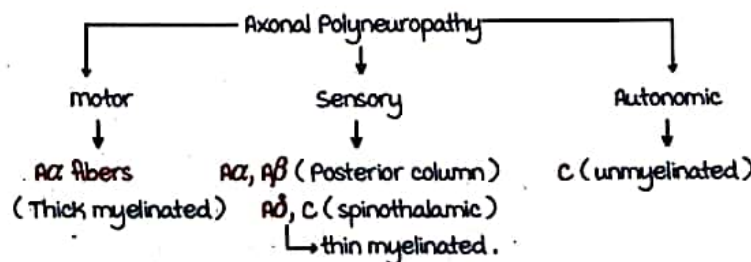
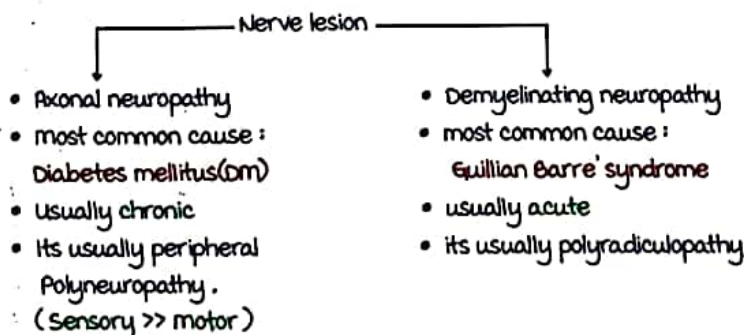
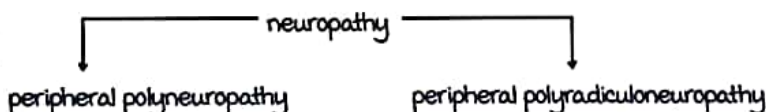
2. location: AHC → grey matter of spinal cord

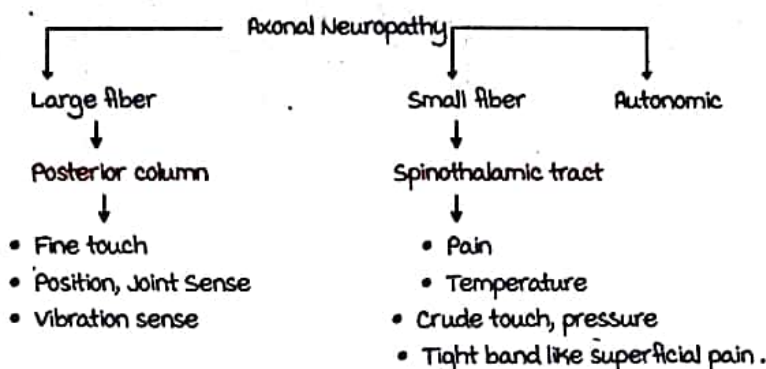
cranial nerve nuclei → brain stem

- | | |
|---|----------------|
| <ul style="list-style-type: none"> • Dorsal root ganglion - Ganglionopathy • Spinal nerve root (dorsal + ventral root) - Radiculopathy • Plexus - Plexopathy • Nerves - mononeuropathy • mononeuropathy multiplex - Polyneuropathy • Neuromuscular Junction • muscle | Neuronopathies |
|---|----------------|

Neuropathy

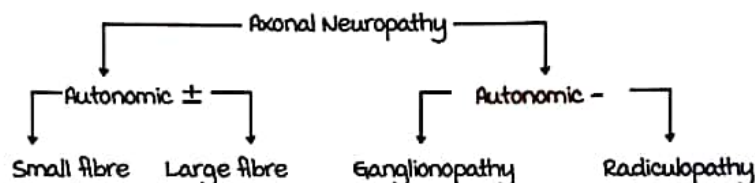
00:09:55





Axonal neuropathy

00:17:05



- Small fibre : Chronic disease
 - Small fibre >> motor fibres
- Large fibre : Posterior column >> motor
- Ganglionopathy : Pure posterior column involvement
Typically characterised by Truncal and Sensory ataxia
- Radiculopathy : Assymetrical, pain along the Root.
Reflexes Lost.

Small fibre neuropathy

00:20:03

causes :

most common cause : DM > Leprosy > Amyloidosis

Tangier's disease

Fabry's disease - maximum pain

HIV

Vasculitis

SLE, CTD (Connective Tissue Disease)

Arsenic poisoning.

Clinical Presentation :

- chronic axonal small fibre polyneuropathy
- loss of key sensations such as : Pain, temperature, Crude touch and Pressure.

- Patients feel characteristic burning pain due to Regenerating nerves .
- Symmetrical involvement
- Evolution : distal to proximal - Glove and stocking or Dying back Neuropathy
- minimal motor Symptoms
- Reflexes intact .
- Posterior column - intact .
- In early stages - nerve conduction - normal .
- In late stages - decrease in amplitude of motor / sensory action Potentials .
- Allodynia : non - noxious stimulus causes pain .
- Foot ulcers .

Large fibre neuropathy

00:25:22

Causes :

A. Vitamins

- Vitamin B₁₂ ↓ - most common cause .
- Pyridoxine Toxicity

B. Drugs :

- Cisplatin , Taxanes
- Friedreich's Ataxia
- Paraneoplastic Syndromes .

Clinical Presentation :

- Chronic axonal large fibre polyneuropathy
- Distal to proximal evolution
- Pins and needles, tingling, numbness and paresthesias
- Sensory ataxia
- Diminished reflexes
- motor findings - minimally present
- Nerve conduction studies - findings are more apparent .
Axonal - decrease in amplitude .

Ganglionopathy and Radiculopathy

00:32:21

Ganglionopathy :

Causes : Sjogren Syndrome - most common cause .

Paraneoplastic Syndromes - Anti - Hu Antibodies
(Small cell ca . of lung)

- rare causes: cisplatin ; vitamin B₆ toxicity ; HIV

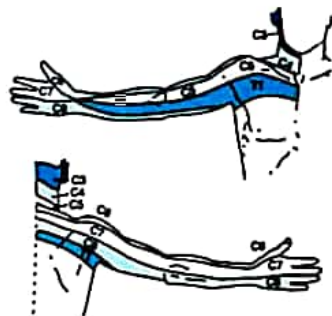
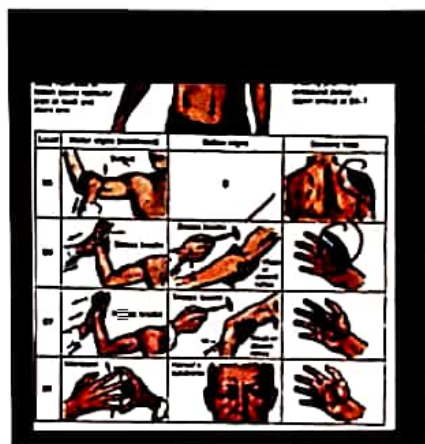
Clinical Presentation :

- Only Posterior Column is involved . - Truncal part
- Severe disproportionate sensory ataxia

- Radiculopathy :
 - Asymmetrical
 - Root pain along the distribution .
 - Reflexes - lost
 - muscles of that particular radicle is involved .
- Eg : If L_4 root is involved (L_4 radiculopathy)

↓
Supplies both Obturator and Femoral nerve

↓
Adduction of Hip and Extension of knee - both are affected .



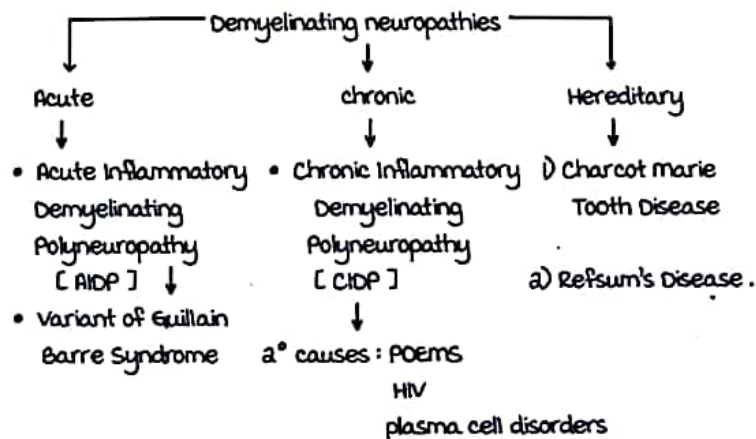
Combined small and large fibre neuropathy

Causes :

- Carcinomatous
- D.M
- Primary biliary cirrhosis
- Hereditary

Demyelinating neuropathies

00:39:28



Differences between Axonal and Demyelinating neuropathies :

AXONAL	DEMYELINATING
• mostly chronic • Polyneuropathy • Distal → proximal progression • Reflexes - spared. (unless it's large fibre neuropathy) • CSF : proteins - normal. • Sensory >>> motor • Wasting - minimal • Nerve Conduction study [NCS] - Amplitude affected • ANS ±	• mostly Acute • Polyradiculoneuropathy • diffuse proximal + distal • reflexes - lost • CSF : Proteins - ↑ • Sensory - mild posterior column findings • motor >>> Sensory • Conduction velocity - ↓ • Distal latency affected. • ANS ±

Motor predominant neuropathies

00:45:20

Causes : AIDP - GBS

Acute Intermittent porphyria

Diphtheria

Lead intoxication

Hereditary motor sensory neuropathy

Diabetic polyradiculoneuropathy / diabetic amyotrophy

Predominant autonomic findings :

- GBS - AIDP
- DM
- Amyloidosis
- Porphyria
- Paraneoplastic
- Drugs : Vincristine, Cisplatin, Amiodarone.
- HIV.

Patterns of presentation

00:49:40

- Symmetrical proximal and distal weakness with sensory loss - Demyelinating disease. Eg : AIDP
- Symmetrical distal sensory loss with or without weakness - Axonal small fibre neuropathy.
- Asymmetrical distal weakness with sensory loss - mononeuritis multiplex or radiculopathies

- Asymmetrical proximal and distal weakness with sensory loss - Polyradiculopathy or plexopathy.
- Asymmetrical Distal Weakness without Sensory loss - amyotrophic lateral sclerosis (ALS) or multifocal motor neuropathy (MMN).
- Symmetrical Sensory loss with distal areflexia and UMN features - Vit B₁₂ / E / copper. ↓
- Symmetrical weakness without sensory loss - muscle disorders or Rarely anterior horn cell disorders like spinal muscular atrophy.
- Asymmetric proprioceptive loss without weakness - ganglionopathy

Differences between demyelinating and Axonal disorders 00:56:38

Based on nerve conduction study (NCS)

	Axonal	demyelinating
1. Amplitude - sensory / motor	decreased	normal
2. Distal latency	normal	prolonged
3. Conduction velocity	normal	slow
4. Conduction block	absent	present
5. Temporal dispersion	absent	present
6. F-wave	normal	prolonged.
7. H-reflex	normal	prolonged.

F Wave :

- In Axonal pathology - No value for F-wave as the common motor Action Potential - [CMAP] is already reduced.
- In Early demyelinating pathology - CMAP - normal

↓
F wave latency prolonged.

H-reflex :

- It is equivalent to S₁ root / Ankle jerk.
- In Early demyelination - H-reflex prolonged.

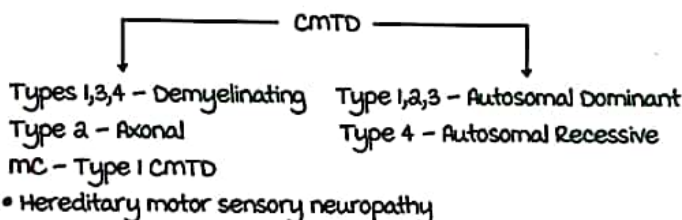
PERIPHERAL NEUROPATHY: INHERITED AND ACQUIRED

Inherited peripheral neuropathies :

1. Charcot marie tooth disease
2. Familial Amyloid polyneuropathy
3. Porphyria
4. Fabry's
5. Refsums disease
6. Tangiers disease

Charcot Marie Tooth Disease (CMTD)

00:01:33



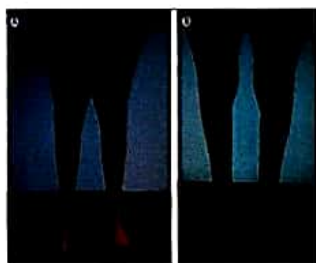
Clinical features :

- Long , slow progressive history of weakness and muscle wasting
 - Foot deformity : Pes cavus in an adult
 - No definite sensory symptoms but definite large fiber sensory signs present.
 - Distal muscles involved , proximal muscles spared .
 - Uniformly slow motor conduction velocities - Demyelinating disease
- (in acquired cause - patchy slowing)

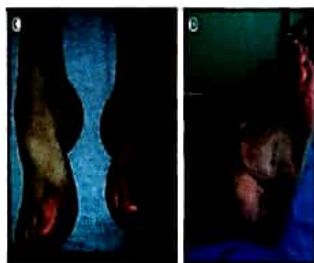
On examination :

- Deep tendon reflexes : Ankle jerks absent
frequently associated with hypo / areflexia
- Upper limb involvement - in later 2/3rd of life .
- Distal muscles involved
and proximal muscles spared
↓
• Inverted champagne legs .

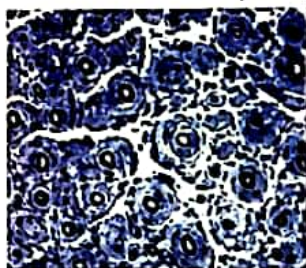
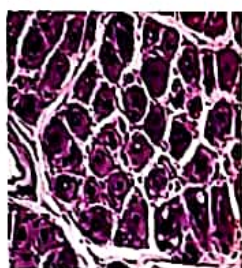
Inverted champagne legs



pes cavus



On Biopsy : Onion Bulb appearance - most classically in Type I



- Other Deformities : Hammer toe , mild kyphosis in nearly $1/10^{\text{th}}$
- Enlarged palpable : Hypertrophic peripheral nerves - in $1/4^{\text{th}}$.
- Roussy - Levy syndrome : Hereditary motor sensory neuropathy + upperlimb postural tremors .

CMTD - Type 2 :

- Later in onset
- Axonal pathology
- Deformities - less prominent
- No nerve enlargement .
- No upper limb involvement .

CMTD - Type 3 :

- Aka Dejerine Sottas Disease - AD
- Childhood onset .
- Severe disability
- Delayed motor development

Familial amyloid polyneuropathy and porphyrias

00:10:03

Familial Amyloid Polyneuropathy :

- Inherited Transthyretin gene mutation
- Small fiber sensory >> motor axonal neuropathy

- ANS Symptoms + + +
- Numbness and painful paresthesias .

Porphyria :

- Only 3 forms of porphyria causes neuropathy .
- Acute Intermittent Porphyria - No cutaneous manifestations
- Hereditary coproporphyria
- Variegate porphyria .

} Cutaneous manifestations + +



Blisters , Hyperpigmentation .

- AD mode of inheritance
- First attack : 30 - 40 years of life .
- Female > male
- G . I . symptoms : abdominal pain, nausea, vomiting
- Severe ANS symptoms + + +

Neuropathy in porphyria :

- Subacute in onset
- Proximal upper limb predominant motor neuropathy .
(arm - affected first)
- Rapidly progressing muscle wasting
- Facial and bulbar involvement
- GBS like presentation
- Severe ANS Symptoms + + +
- Sensory involvement - Bathing suit pattern .

Fabry's , Tangier's and Refsums disease

00:15:05

Fabry's disease :

- XLR - α - galactosidase deficiency
- Onset : childhood
- Painful small fiber axonal neuropathy
- Distal paresthesia and lancinating pain
- ANS symptoms + + +
- Angiokeratomas + painful acral paresthesias .

Tangier's disease :

- AR/ATP binding cassette protein defect
- Reduced HDL
- Asymmetrical mononeuropathy
- Orange tonsils
- Axonal degeneration

Refsums disease :

- Peripheral neuropathy + retinitis pigmentosa + cerebellar ataxia .
- Defect in α - oxidation of fatty acids due to deficiency of an enzyme called Phytanic acid oxidase

Acquired neuropathies

00:19:05

• Acquired demyelinating neuropathies :

- AIDP
- CIDP

Axonal acquired neuropathies :

- MCC of Acquired axonal neuropathy : Diabetes mellitus

Diabetes mellitus :

- MC type of neuropathy in DM : Small fiber sensory >> motor neuropathy
- Symmetrical , length dependant
- Distal to Proximal .
- Dying back /Glove and stocking neuropathy
- ANS symptoms + + +
 - Gustatory sweating
 - Nocturnal diarrhea

Other forms of Diabetic Neuropathy :

- Large fiber neuropathy
- Cranial Nerve Neuropathy : Pupil sparing 3rd Nerve Palsy > 6th Nerve palsy
- Diabetic Amyotrophy : Lumbo sacral radiculoplexopathy.
 - Unrelated to diabetic control
 - Asymmetrical -
 - Pain along the distribution of radicle
 - Proximal lower limb pain and weakness .
 - If L₄ involved → Knee jerk absent
 - Distal lower limb - not involved
 - associated with Weight loss .
- For radiculopathies → SLR + ve (Straight Leg Raising Test)
- mononeuropathies can also occur in the form of carpal tunnel syndrome .

Primary light chain amyloidosis

00:28:13

- AL Amyloidosis
- Small fiber distal symmetric sensory polyneuropathy followed by large fiber involvement

- ANS Symptoms + + +
- $\lambda \gg \kappa$ chains
- MCC of death : cardiac failure
- MCC of restricted cardiomyopathy : Amyloidosis.

HIV Neuropathy

00:30:26

Different type of neuropathies in HIV :

- MC : diabetes like neuropathy
- GBS or CIDP like pattern
- Sensory ganglionopathy
- Polyradiculopathy : most common in CMV infection.
- Mononeuritis multiplex - associated with medium vessel vasculitis
- In small fiber sensory neuropathy - Pain and temperature are affected more.

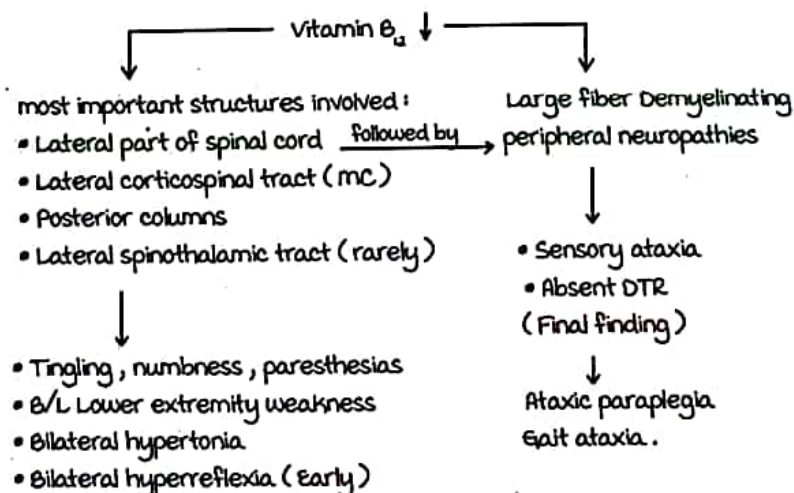
Critical illness polyneuropathy

00:33:31

- Seen in sepsis/ MODS - in ICU patients (> 7 days)
- Suspected when there is difficulty in weaning off from ventilator
- Distal axonal sensorimotor neuropathy
- Severe flaccid weakness of both extremities.

Subacute combined degeneration of spinal cord

00:35:00



Paraneoplastic, autoimmune and vasculitic causes of neuropathy

00:41:00

Paraneoplastic neuropathy:

1. Sensory → Ganglionopathy → Small cell Lung Cancer → anti Hu antibodies
2. Subacute motor Neuropathy → Asymmetric, proximal upper limb
↓
predominant
Associated with Lymphoma
3. Cerebellar findings → gynecological malignancies → antibodies.

Autoimmune and Vasculitic causes:

- SLE, Scleroderma, Rheumatoid arthritis, Vasculitis → DM like small fiber Neuropathy.
- Sjogren → ganglionopathy
- Medium vessel vasculitis → mononeuritis multiplex
- Vasculitis: Severe neuropathy → Churg Strauss > Wegeners.
- Large vessel vasculitis do not produce neuropathy.

Charcot's disease, botulism

00:45:06

Charcot's disease:

- Severe form of neuropathy leading to progressive destructive arthritis
- Neuropathic joint disease
- Most common cause: DM > Amyloid > Leprosy > Tabes Dorsalis > Syringomyelia
- Most commonly affected joints: medial tarsometatarsal joints
- Most common type: Atrophic type > Hypertrophic type.

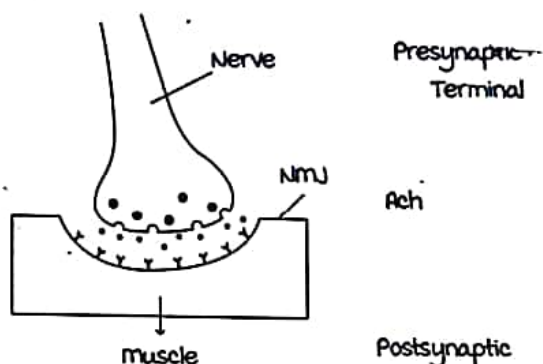
Botulism:

- Symmetrical cranial nerve palsy
 - Flaccid descending symmetrical palsy
 - Deep Tendon Reflexes - preserved
 - Nausea, Vomiting, Abdominal pain with autonomic dysfunction
 - Fever
 - Sensory symptoms
 - Mentation - intact.
- } Absent

NEUROMUSCULAR JUNCTION

Myasthenia Gravis

00:00:58



Pathophysiology:

1. Decrease in number of Acetylcholine receptors in the post synaptic membrane
2. Acetylcholine cannot bind to receptors

→ Blocking antibodies and destructive antibodies

→ myasthenia gravis is Tcell + Bcell mediated

→ TH2 mediated activation of Tcell → produces IL-4

↓
Stimulates B-cells

↓
Produces antibodies

↓
Produces disease

• Autoimmune disease with HLA association

• majority population has thymus pathology

→ Produces T cells

Seropositive myasthenia gravis

→ Antibodies positive

→ Anti acetylcholine receptor antibody (most specific)

Active space

Seronegative myasthenia gravis

1. Anti musk antibody (muscle specific kinase)
2. Anti Lipoprotein receptor - 4
3. Anti striated muscle antibody

1. Ocular myasthenia → 50% seropositive

- Anti musk antibody

2. Generalized → 80 - 90% seropositive

- 75% → Thymus involvement
- 65% → Thymic hyperplasia
- 10% → Thymoma

Clinical features of myasthenia gravis

00:08:34

Age group : Bimodal

- Early onset → second to third decade
Females more common than males
→ Associated with other autoimmune disease → Hashimoto's thyroiditis, Addisons, pernicious anemia, vitiligo, Type 1 DM
- Late onset → sixth to seventh decade
→ Incidence : males = females
→ Absence of thymus involvement
→ HLA DR2, LPR4
→ Antibodies → Antiacetylcholine receptor antibody, Titin, Ryanodine
→ Oropharyngeal and facial involvement
→ myasthenia gravis starts as ocular presentation then generalized
→ Fluctuating weakness and fatiguability
- Weakness is more on repeated activity
→ Starts with ocular or pharyngeal then goes to generalized weakness → proximal muscles of lower limb → Pharyngeal/Bulbar → Respiratory muscles
Late → respiratory involvement
→ Early onset myasthenia
→ F > M
Anti Acetylcholine receptor Antibodies +++
Thymic hyperplasia
HLA - DR3, DR9, B8

Anti musk antibody

00:17:01

- Seen in ocular myasthenia
- Seen in 40 to 50% cases of Seronegative myasthenia
- Thymus not involved
- Females > males
- Characterized by → severe oropharyngeal / buccal and facial involvement
- Tongue fasciculations are seen
- Proximal muscles and neck muscles are spared
- Refractory to standard therapy

Clinical presentation :

- Ocular
 - Ptosis with diplopia (Classical presentation)
 - Fluctuating with fatiguability
 - variable degree of ptosis
 - Ptosis can be unilateral or bilateral and asymmetrical
 - Binocular diplopia with sparing of pupils
 - Earliest ocular muscle affected → medial rectus
 - Cogan's lid twitch
- Pharyngeal
 - Dysphagia, dysarthria, nasal regurgitation, fatigue on chewing
 - ± Facial muscles (musk antibody)
 - Expressionless facies
- Proximal weakness of upper limb muscles (Lower limb weakness > upper limb)
 - Neck weakness → drooped posture
 - Proximal muscle of lower limb
 - Typically hip muscles
- Respiratory muscle involvement

Differential diagnosis of myasthenia gravis

00:24:22

- Chronic progressive external ophthalmoplegia
 - mitochondrial myopathy
 - Only ptosis present, no diplopia
 - No pharyngeal muscle involvement
 - No bulbar muscle involvement

Always examine →

- Severity of weakness
- Double vision on lateral gaze, ptosis, lid closure
- Swallowing

- Speech
- Hand grip for distal muscles
- Arm outstretched for proximal muscles
- Head lift for neck muscles
- Vital capacity for respiratory muscles

Diagnosis →

Ice pack → Improves weakness

Tension test (edrophonium) → Dose of edrophonium for tension test - 2 mg

Specific → Acetylcholine receptor antibody

Sensitive → Repetitive nerve stimulation tests (decremental response in amplitude of compound motor action potential)

- Single nerve fibre electromyography
→ Increased jittering

Lambert Eaton myasthenic syndrome

00:31:27

- Paraneoplastic condition associated with small cell carcinoma of the lung
- Antibody against Presynaptic V/Q calcium channel receptors
- Proximal lower limb weakness with only mild diplopia and ptosis
- Reflexes absent
- ANS findings (+++)
- Nerve conduction study → incremental response on repetitive nerve stimulation
- Dois sign
- 3, 4, Diamino pyridine useful

Treatment of myasthenia gravis :

- Pyridostigmine : 30-60 mg → 6th hourly, later taper off
- Relapse → Steroid ± Azathioprine
- Crisis → Respiratory crisis → IV Ig and PLEX (plasma exchange)

Cholinergic crisis :

- D → Diaphoresis
- U → Urination excess
- M → miosis
- B → Bradycardia
- B → Bronchial secretions
- E → Emesis
- L → Lacrimation
- L → Loose stools

Active space

Role of IV Ig or PLEX:

- myasthenia crisis → respiratory insufficiency, dysphagia
- Refractory myasthenia
- Surgery (bulbar dysfunction)
- musk positive cases → refractory to cholinesterase inhibitors

Thymectomy

00:38:02

Indications:

- Thymoma → associated with hypogammaglobulinemia
= Good's syndrome
- Acetylcholine receptor antibody positive and generalized myasthenia → 18-65 years
- musk positive, elderly, ocular myasthenia → Thymectomy is not indicated

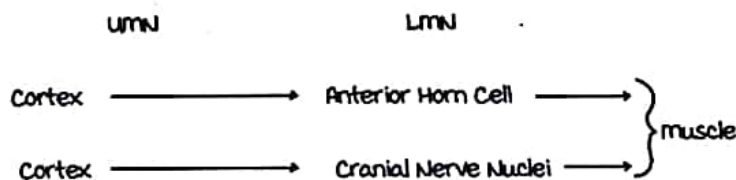
Drugs that precipitate myasthenia:

- d- Pencillamine
- Procainamide
- β - blockers
- Amino glycosides
- Quinolones
- macrolides
- Azathioprine

Congenital myasthenic syndromes

- Slow channel → most common
- Autosomal dominant

APPROACH TO MYOPATHY



LMN pathology: Lesion in the

1. Anterior Horn cell:

- No Sensory / ANS / cerebellum involvement
- Asymmetrical involvement
- Wasting
- Fasciculations, atrophy + + +
- Distal muscles > proximal muscles
- Eg: motor Neuron Disease
 - Spinal muscular Atrophy
 - Hirayama's Disease
 - Intramedullary - Syringomyelia

2. Dorsal root ganglion:

- Ganglionopathy
- Only Posterior Column involved
- Severe disproportionate Sensory Ataxia
- Causes: Sjogren syndrome
 - Paraneoplastic - Small cell carcinoma of Lung
 - Anti-Hu Antibodies

3. Radiculopathy: Spinal Nerve Root

- Asymmetrical
- Root pain along the distribution of nerve
- Sensory, motor and reflexes - Lost
- Muscles of that particular nerve root is involved
- Eg: If L₄ radiculopathy → L₄ Supplies both obturator and femoral Nerve → Both adduction of Hip and extension of knee are lost.

4. Plexus - plexopathy

5. Peripheral Nerve - Sensory ± motor

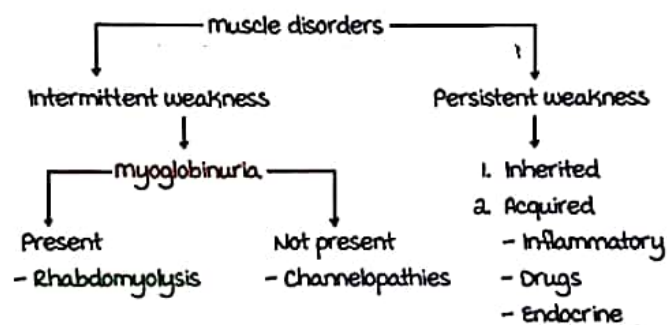
- Distal to proximal evolution

6. Neuromuscular junction :

- Fatigability
- Fluctuating weakness
- Ocular problems
- Pharyngeal muscle problems

7. muscle :

- Purely motor
- Completely symmetrical
- Almost always proximal, predominantly lower limb .
- No wasting usually
- Reflexes - normal .



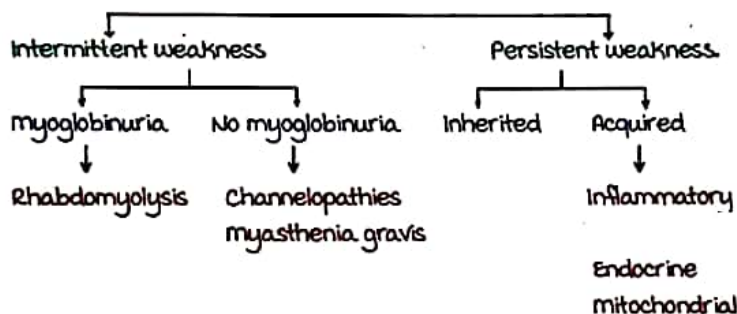
MYOPATHY

Myopathies

00:00:09

- LMN type of pure motor weakness.
- Proximal weakness >> distal weakness.
- No wasting / no atrophy / no fasciculations.
- Reflexes preserved.
- No involuntary movements.
- No sensory loss.
- ANS - normal.

Types of myopathy.



Difference between Anterior horn cell and muscle.

Feature	Anterior horn cell	muscle
Weakness and wasting	wasting >> weakness	weakness > wasting
Symmetric	Asymmetric	Symmetric
Distribution	Distal > proximal	proximal
Reflexes	Absent	Late hyporeflexia, proportionate
Involuntary movements	Fasciculations present	absent

Symptoms of a muscle disorder classification.

- | | |
|--|---|
| Positive symptoms
(1) myalgia
(2) Cramps
(3) Contractures
(4) myotonia
(5) myoglobinuria | Negative symptoms
(1) weakness
(2) Fatigue
(3) Exercise intolerance |
|--|---|

Active space

Symptoms of muscle disorder

00:04:26

① Weakness :

- Proximal lower extremities.
 - Difficulty in climbing stairs, rising from a low chair or toilet, or getting up from a squatting position.
- Proximal upper extremities.
 - trouble in lifting objects over the head and brushing the hair.
- Distal upper extremities.
 - difficulty in opening jars, inability to turn a key in the ignition.
- Distal lower extremities.
 - ... tripping due to foot drop.

② Fatigue and Exercise intolerance

- Non specific symptom.
- Abnormal fatigability even after minimal exercise without involving sensory / autonomic nervous system



" Inflammatory muscle disorders "

3 myalgia

① Non specific symptom

- Extremely uncommon for a myopathy to cause vague aches and muscle discomfort in presence of a normal neuromuscular examination and laboratory studies.
- Fibromyalgia vs polymyalgia rheumatica.

Fibromyalgia	Polymyalgia rheumatica
- Severe muscle pain - Pain in trigger points. - Easy fatigability - Normal ESR - Normal muscle enzymes - NSAIDs	- Occurs in giant cell arteritis. - associated with HLA-DRB1*04 - 04 gene - Pain and stiffness in - Hip, shoulder, pelvic girdle - ESR > 50mm / hr - 100 % responsive to steroids. - Normal muscle enzymes.

4 muscle cramps.

- Not a feature of myopathy except Duchenne muscular dystrophy

① Causes : - Dehydration

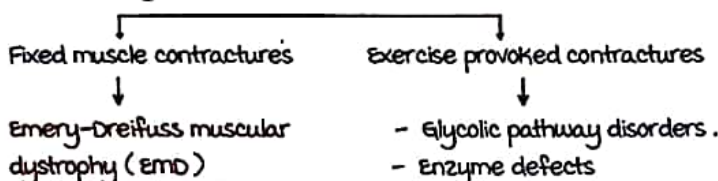
- Hyponatremia

- Azotemia

- myxedema.
- Disorders of the nerve or motor neuron.
(especially amyotrophic lateral sclerosis)
- Renal failure.

5 muscle contractures.

- ⑤ contractures differ from cramps → they last longer and are electrically silent with needle EMG.



- Contractures are uncommon.

6 myotonia

- ⑥ The phenomenon of impaired relaxation of muscle after forceful voluntary contraction.
- mc involves hands and eyelids.
- occurs due to repetitive depolarization of the muscle membrane.
- Conditions showing myotonia:
 - 1) myotonic dystrophy
 - 2) myotonia congenita
 - 3) Hyperkalemic periodic Paralysis.
- myotonia improves with exercise
- Exposure to cold - worsens both myotonia & paramyotonia
- Paramyotonia
 - Seen in paramyotonia congenita
 - worsens with exercise.
- In myotonia patients complain of muscle stiffness resulting in difficulty to:
 - 1) releasing handgrip after hand shake
 - 2) Opening eyelids if they forcefully shut their eyes.
- myopathies present at birth

Congenital myopathies

seen in 1) Central core myopathy.

2) Centronuclear myopathy.

3) Nemaline myopathy.

4) Congenital myotonic dystrophy.

Duchenne Muscular Dystrophy [DMD]

00:16:58

- X - linked recessive , progressive muscle degeneration .
- dystrophin gene mutation
- onset before 5 years . (3-5 years)
- proximal lower limb muscles affected (mc)
- presentation : - frequent falls .
 - Lumbar Lordosis
 - Protuberant abdomen .
 - Waddling gait .
 - mental retardation (IQ)
- milestones -
 - 6 years → Toe walking with heel cord contracture .
 - 12 years → wheel chair bound .
 - 16 - 18 years → Recurrent pulmonary infection death (mc cause)
- Complications :
 - Pseudohypertrophy of calf muscles .
 - Scoliosis → impairment of lung functions

↓

recurrent pulmonary infections .

 - Cardiomyopathy (Dilated cardiomyopathy)

↓

Conduction abnormality .

- management : Steroids (limited use)
- limb - girdle weakness
 - ↓
 - " Gower's sign "
 - Observed when child arises from supine position .

**Becker's muscular dystrophy & Limb girdle muscular dystrophy**

00:21:32

Becker's muscular dystrophy .

- X linked recessive .
- dystrophin gene mutation .
- Enzymes , EMG, Biopsy → similar for both DMD and Beckers .
- Variable disease onset . (5-60 yrs)
- Survival upto 4th decade
- No mental retardation
- No contractures .

- mc cause of death → Cardiomyopathy.
- Steroid work better in Becker's dystrophy

Limb girdle muscle dystrophy.

- mc type of adult onset muscle dystrophy.

Types :

Type I

Autosomal dominant
Protein : Caveoline

Type II

Autosomal recessive
protein : α A : Calpain
 α B : Dysferlin
- Occurs in 2nd decade.

- Early onset limb girdle muscle dystrophy due to

↓
Alpha dystroglycan protein (within 10 years)

- Late onset limb girdle muscle dystrophy due to

↓
Desmin protein.

Calpainopathy

- Early finding : "Scapular winging"

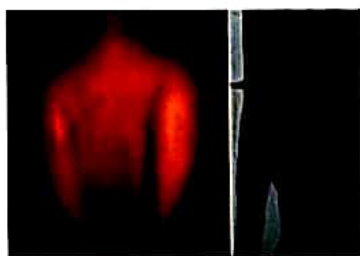
Causes :

- Scoliosis
- wrist, elbow and finger contractures.
- Achilles tendon contractures

↓
Causes toe walking.

- Proximal lower limb muscles affected.

↓
Severely affected : Hip adductors



Dysferlinopathy

- mutation in dysferlin gene located in chromosome 12p13.
- Important in membrane repair.
- Presents in adolescence or early adulthood.
- Slow progression.
- Diamond sign of thigh

↓
Occurs due to selective muscle wasting of vastus lateralis and rectus femoris in their upper and lower part with muscle sparing of the middle part portion.



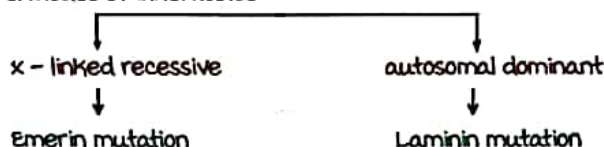
- mc affects gastrocnemius and hamstrings.

Emery dreifuss syndrome and Fascio scapulo humeral muscle dystrophy

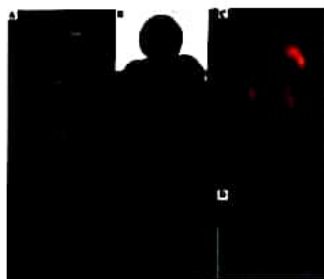
00:29:04

Emery dreifuss muscle dystrophy.

- 2 modes of inheritance



- Prominent contractures
- muscles involved
 - Humoral
 - Peroneal
- Cardiomyopathy
- Colour blindness.



Fascioscapulohumeral muscle dystrophy.

- Autosomal dominant
- Severe in males
- Childhood onset
- Involves chromosome 4q
- Childhood facial weakness followed by weakness of shoulder girdle.
- Winging of scapula on abduction
- Biceps, triceps affected
- Deltoid spared.
- If lower limb involvement → Distal limb and ankle dorsiflexion affected.
- Associated with:
 - Nerve deafness
 - Coats disease
 - Colour blindness
- Facial, shoulder and scapula girdle seen.
- No cardiomyopathy.



FIGURE 40-1 Fascioscapulohumeral dystrophy with prominent scapular winging

Myotonic dystrophy

00:34:50

- 2 Types.
- DM₁ - Type 1 → Distal muscle weakness (mc)
- DM₂ - Type 2 → Proximal muscle weakness. (rare)
- Both Type 1 and Type 2

Autosomal dominant, trinucleotide repeat disorders.

Facial involvement →

- Temporalis muscle
- masseter muscle
- Fascial muscle.



Fig. 1: Clinical photographs of patient showing weakness of temporalis muscle, resulting in a flattened jawline and a 'hatchet' facial appearance.

- Hatchet facies and frontal baldness seen.
- muscles of neck involved.
- Sternocleidomastoid (mc)
- Distal upper limb muscle involvement.
- (upper limb involvement >> lower limb involvement)
- Bulbar dysarthria (pharyngeal muscle weakness)
- myotonia → Percussion myotonia
- Respiratory involvement
- Additional findings:
 - 1) Cardiac conduction abnormalities
 - 2) Intell
 - 3) Posterior subcapsular cataract
 - 4) Gonadal atrophy.
 - 5) Insulin resistance.
- management → phenytoin
- For conduction abnormality → Pacemaker.
- Type 1 fibres → selective atrophy.



Fig. 2: "Percussion myotonia" in thenar muscle of hand.

Congenital muscle dystrophy

- 1) Fukutin
- 2) Fukuyama
- 3) merosin deficiency

Distal myopathy

- 1) welander
- 2) Nonaka
- 3) miyoshi

Mitochondrial myopathies

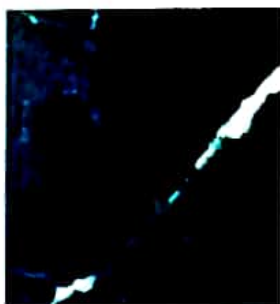
00:43:35

- maternally inherited
- Types :
 - 1) Kearns - Sayre syndrome
 - 2) Chronic progressive external ophthalmoplegia . (CPEO)
 - 3) Pure mitochondrial myopathies .
 - 4) MERRF (myoclonic epilepsy with red ragged fibers)
 - 5) MELAS (mitochondrial encephalopathy, lactic acidosis and stroke - like episodes)
 - 6) Lebers hereditary optic neuropathy .

Inheritance :
maternal / Autosomal
Dominant / Recessive / sporadic

Histopathological finding :

- Biopsy of muscle shows :
'Red ragged fibers'
- Stain used : Gomori trichrome stain



Chronic progressive external ophthalmoplegia (CPEO)

- Presentation → 3rd - 4th decade
- Autosomal dominant or sporadic
- Onset after puberty
- Symmetrical ptosis without diplopia .
- Biopsy Red ragged fibers .
- Sensorineural hearing loss (deafness)

Kearns sayre syndrome .

- Onset : sporadic before 20 years .
- Features :
 - 1) Findings of chronic progressive external ophthalmoplegia
 - 2) Retinitis pigmentosa .
 - 3) complete heart block .
 - 4) cerebellar ataxia .
 - 5) mental retardation .
 - 6) Gonadal dysfunction .
 - 7) Diabetes mellitus .
- On Biopsy : Red ragged fibers seen .

MERRF syndrome and MELAS syndrome

00:49:28

MERRF syndrome :

- myoclonic epilepsy with red ragged fibers .
- Features :
 - 1) mitochondrial myopathy (proximal lower limb weakness)
 - 2) myoclonic epilepsy .
 - 3) Cerebellar ataxia .
 - 4) Dementia
 - 5) Optic atrophy .
- Onset : 10 - 30 years .
- Limb girdle distribution .

MELAS SYNDROME :

- mitochondrial encephalopathy with lactic acidosis and stroke .
- Presentation < 20 years with partial seizures .
- Stroke like without vascular distribution
- Features :
 - Weakness / hemiparesis
 - Hemianopia < 40 years .
 - Lactic acidosis .
 - Point mutation in mitochondrial + - RNA
 - Red ragged fibers .
 - Can be associated with :
 - 1) Hypothalamo pituitary gonadal dysfunction .
 - 2) Basal ganglion calcification

Rhabdomyolysis :

- myoglobinuria with intermittent weakness .
- Causes :
 - 1) muscle phosphorylase deficiency
[Eg : mc Ardle disease - G S D Type 5]
 - 2) Glycolytic pathway defect .
 - 3) Carnitine palmitoyl transferase deficiency .

Electrolyte abnormalities causing episodic weakness :

- Hyponatremia .
- Hypokalemia .
- Hyperkalemia .
- Hypercalcemia .
- Hypophosphatemia .

Active space

Channelopathies

00:58:35

Type	Disease
Calcium	Episodic ataxia type 2 Spinocerebellar ataxia type 6 Hypokalemic periodic paralysis familial hemiplegic migraine
Sodium	Hyperkalemic periodic paralysis paramyotonia congenita normokalemic periodic paralysis
Chloride	Myotonia congenita
Potassium	Episodic ataxia type 1 benign neonatal familial convulsions

1) Calcium channelopathies [E_aS₆ HOM]

- Episodic ataxia type 2
- Spinocerebellar ataxia type 6.
- Hypokalemic periodic paralysis
- Familial hemiplegic migraine.

2) Sodium channelopathies.

- Hyperkalemic periodic paralysis.
- Normokalemic periodic paralysis Paramyotonia congenita.

3) Chloride channelopathies.

myotonia congenita.

4) Potassium channelopathies.

- Episodic ataxia type 1.
- Andersen-Tawil syndrome.
- Benign neonatal familial convulsions.

Hypokalemic/Hyperkalemic periodic paralysis
and Andersen-Tawil syndrome

01:01:47

Presentation : Acute onset, intermittent, bilateral weakness.

	Calcium Channel	Sodium Channel	Potassium Channel
Feature	Hypokalemic PP	Hyperkalemic PP	Paramyotonia Congenita
Mode of inheritance	AD	AD	AD
Age of onset	Adolescence	Early childhood	Early childhood
Myotonia	No	Yes	Yes
Episodic weakness	Yes	Yes	Yes
Frequency of attacks of weakness	Daily to yearly	May be 2-3/d	With cold, usually rare
Duration of attacks of weakness	2-12 h	From 1-2 h to >1 d	2-24 h
Serum K ⁺ level during attacks of weakness	Decreased	Increased or normal	Usually normal
Effect of K ⁺ loading	No change	Increased myotonia, then weakness	Increased myotonia
Effect of muscle cooling	No change	Increased myotonia	Increased myotonia, then weakness
Fixed weakness	Yes	Yes	Yes

*Dysmorphic features and cardiac arrhythmias are distinguishing features (see text). May be paradoxical in paramyotonia congenita. Abbreviations: AD, autosomal dominant; PP, periodic paralysis.

Channelopathies

00:58:35

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myotonia congenita.

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Hypokalemic/Hyperkalemic periodic paralysis and Andersen-Tawil syndrome

01:01:47

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Effect of K ⁺ loading	No change	Increased myotonia, then weakness	Increased myotonia
Effect of muscle cooling	No change	Increased myotonia	Increased myotonia, then weakness
Prolonged weakness	Yes	Yes	Yes

*Dysmorphic features and cardiac arrhythmias are distinguishing features (see text). May be paroxysmal in paramyotonia congenita. Abbreviations: AD, autosomal dominant; PP, periodic paralysis.

Features	Hypokalemic periodic paralysis	Hyperkalemic periodic paralysis	Andersen-Tawil syndrome
Channelopathy	Calcium	Sodium	potassium
Inheritance	AD	AD	AD
Onset	Early adulthood (< 25 years)	Childhood	Childhood
Serum potassium	Low	Normal to high	Variable
myotonia	absent	Present	absent
ECG changes	Changes of hypokalemia.	Normal	Arrhythmia (↑ QT interval)
Facies	Normal	Normal	Dysmorphic

Hypokalemic periodic paralysis.

- Autosomal dominant.
- Onset : adolescence < 25 years
- male > Female
- Precipitated by : High carbohydrate meal.
- Pure proximal limb weakness, no myotonia.
- Hypokalemia during episodes.
- Propensity for arrhythmia.
- management.
 - Never treat with IV potassium.
 - Oral potassium.
 - Acetazolamide.

Hyperkalemic periodic paralysis.

- Autosomal dominant.
- Presentation : first decade. (< 10 years)
- Sodium channelopathy.
- Normal potassium during attacks.
- Proximal muscle weakness.
- Precipitated by : Rest.
- myotonia

Andersen-Tawil syndrome

- Potassium channel disorder.
- Due to inward rectifying potassium channel.
- Dysmorphic features.
- Cardiac arrhythmias
- prolonged QT interval.

Drug induced myopathies

01:11:27

Drugs causing :

(1) Acute onset Rhabdomyolysis .

- Heroin
- Alcohol
- amphetamine
- cocaine .

(2) statins can cause :

- asymptomatic rise in CPK .
- myalgia .

(3) Glucocorticoids can cause :

- Acute quadriplegia (acute presentation)
- Proximal muscle weakness (chronic presentation)
- d - Penicillamine → produce autoimmune myopathy (resemble polymyositis)
- Zidovudine → produce mitochondrial myopathy (red ragged fibers)
- Amiodarone, Hydroxy chloroquine → produce painless weakness with autophagic vacuoles on biopsy .

Endocrine myopathies

01:14:50

• Both hypothyroidism and hyperthyroidism induced myopathies are :

- Proximal myopathies
- Normal EMG

Hypothyroidism induced myopathy

- muscle cramps , pain and stiffness
- Pure proximal myopathy
- Creatine Kinase ↑ ↑
- No fasciculations

Hyperthyroidism induced myopathy

- Asymptomatic
- Proximal + bulbar + esophageal .
- Normal creatine Kinase .
- Fasciculations + +

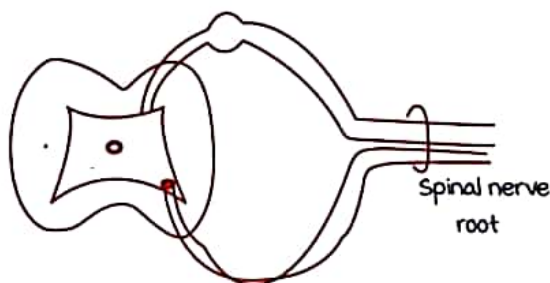
Active space

GUILLAIN - BARRE SYNDROME

Guillain - Barre syndrome

00:01:09

- Types :
1. Acute inflammatory demyelinating polyneuropathy (AIDP) → most common
 2. Acute motor axonal neuropathy (AMAN)
 3. Acute motor sensory axonal neuropathy (AMSAN)
 4. Miller - Fischer syndrome
- mean age → 40 years (no particular age)
 - males are more commonly affected
 - 4 weeks duration (monophasic)
 - more than 4 weeks → Sub acute
 - ~~more than 8 weeks~~ → Chronic
 - molecular mimicry → cross reacting antigens → myelin (M.C.)
 - Antecedent infections → 70% cases
- Triggers :
- Campylobacter jejuni (M.C.)
 - ↳ diarrhoea
 - CMV
 - EBV
 - Mycoplasma
 - Hep. A, B, HIV
 - Zika virus



- Acute inflammatory polyradiculoneuropathy
 - radicular pain (back pain) with tingling, numbness etc.
 - 2 - 3 days prior to weakness
- Proximal and distal weakness which starts in lower limb
 - then upper limb → Brain stem
- Respiratory muscle involvement in 30%
- Areflexia, flaccidity, paraparesis going into quadriplegia
- Sensory signs minimal → posterior column

Active space

- Autonomic nervous system (ANS) involvement
- Bowel bladder symptoms may be seen
- No cerebellar findings
- No higher mental functions involvement
- Cranial nerve palsy as disease progresses
 - Starts with IX, X, XI, then VII then III, IV, VI

Diagnostic criteria for Guillain - Barre syndrome

00:10:37

- Features required for diagnosis
 - Progressive weakness in both arms and legs
 - Areflexia
- Features strongly supporting diagnosis
 - Progression of symptoms over days, up to four weeks
 - Relative symmetry of symptoms
 - Mild sensory symptoms or signs
 - Cranial nerve involvement III, VII
 - Recovery beginning two to four weeks after progression ceases
 - Autonomic dysfunction
 - Absence of fever at onset
 - High concentration of protein in cerebro-spinal fluid, with fewer than 10 cells per cubic millimeter
- Typical electrodiagnostic features
 - Prolonged or absent F/H, temporal dispersion, distal latency, decreased conduction velocity, blocks
- LP → albuminocytologic dissociation
 - Increased CSF protein
 - less than 10 cells / mm³

Pain due to nerve root inflammation

Features excluding diagnosis :

- Diagnosis of botulism, myasthenia, poliomyelitis or toxic neuropathy
- Abnormal porphyrin metabolism
- Recent diphtheria
- Purely sensory syndrome, without weakness

Electro diagnosis :

most sensitive test in evaluating GBS ;

Patterns :

1. motor conduction block
2. Prolonged distal latencies
3. Temporal dispersion
4. Slowing of nerve conduction
5. Increased F-wave latency

- Electro diagnostic parameters are the most reliable indicators of prognosis

AIDP	→ most common	Antibody anti Gm1 antibodies
AMAN	→ Prognosis same Axonal	anti Gd1a antibodies
AMSAN	→ Poor prognosis Axonal	-
Miller - Fisher syndrome	→ Ophthalmoplegia, Areflexia Ataxia Demyelinating	anti Gq1b antibodies

Bickerstaff's encephalitis

00:16:08

- Brainstem encephalitis → altered sensorium
- Hyperreflexia
- Ophthalmoplegia
- Ataxia
- Anti Gq1b
- Response to PLEX (Plasma exchange)

management of Guillain Barre Syndrome

- No role of steroids
- I.V. Immunoglobulin → 0.4 g/kg for 5 days
- Plasma exchange

Clinical course

- Disease progresses for days to 4 weeks
- Typical course is steady progression to nadir within 2 weeks in most cases and 4 weeks in all cases from onset of paresthesia
- Variable plateau phase
- 10 - 15 % mortality
- 80 - 85 % recovery

Active space

- 60 - 65 % complete recovery
- 10 - 20 % residual disability

Chronic inflammatory demyelinating polyneuropathy 00:21:17

- more than 8 weeks
- Relapsing, remitting pattern
- Steroid responsive
- No antecedent events
- No major autonomic
- Bulbar involvement rare → less than 20%
- Generally idiopathic

Secondary causes :

- HIV
- Hodgkins disease
- Plasma cell disorders (most important)

Pattern : motor + Sensory → • large fibre predominant
(more common) • distal to proximal
• Areflexia

- Tremor is more common in CIDP

Treatment :- Steroids → no response → IVIG
- if no response to iv. Ig

↓
PLEX

Differential diagnosis

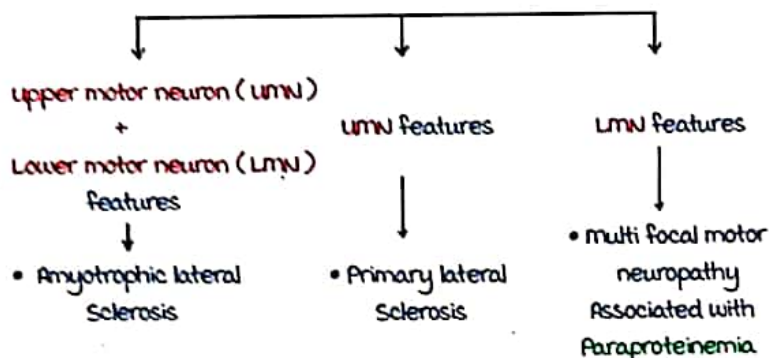
00:27:33

- POEMS
 - P - Polyneuropathy → CIDP
 - O - Organomegaly
 - E - Endocrinopathy
 - S - Skin changes
 - m - multiple myeloma (monoclonal gammopathy)
 - Sclerotic lesions
 - Refractory to therapy

↓
λ (Lamda) chain

MOTOR NEURON DISEASE

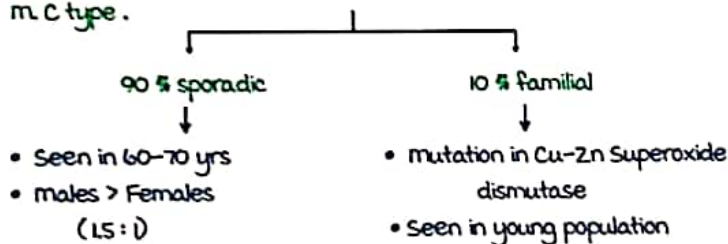
Classification of motor neuron disease



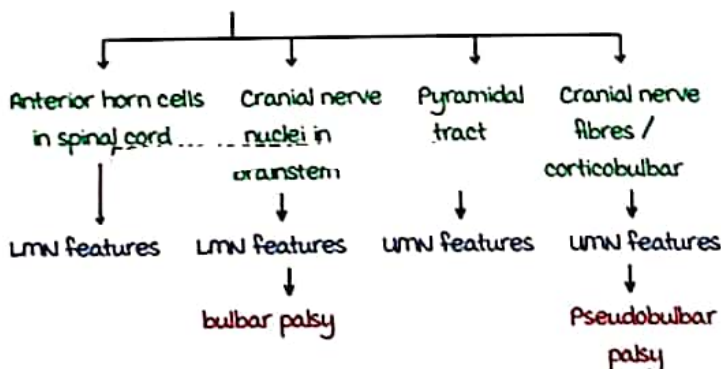
Amyotrophic Lateral Sclerosis (ALS)

00:02:01

m.c type.



ALS is the degeneration of neurons in



Average survival from onset of symptoms : 2.5 - 3.5 years

Amyotrophic lateral sclerosis – symptoms

00:07:59

- In ALS – sensory
 - Higher mental function
 - Extraocular muscle
 - Autonomous nervous system (bowel / bladder)
 - Cerebellum
 } → Not affected / normal
- Asymmetrical onset of symptoms
 - ↓
 - local muscle weakness –
 - ↓
 - distal upper limb weakness
 - ↓
 - Progressive weakness,
 - Wasting of muscle
 - Fasciculations (frequent & multiple localised or generalised)
 - muscle cramps
 - ↓
 - worse at night
 - Eases as disease progresses

Upper motor findings- In amyotrophic lateral sclerosis 00:12:33

- MC finding – Exaggerated or positive reflexes
- ALS – suspected only if LMN + UMN findings are present
- If only asymmetrical
 - ↓
 - Suspect –
 - Multifocal motor neuropathy
 - Hirayama disease (dural buckling) (or) monomelic amyotrophy



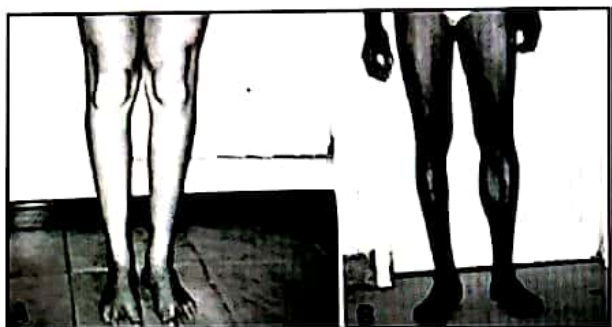


Fig 2. A. Case 20 - Wasting of muscles of right leg. B. Case 3 - Atrophy of right leg and thigh muscles.

- Rarely facial weakness
 - Neck extension affected - Drooped head Syndrome
 - Respiratory muscle involvement
- } → involved at the final stages

Amyotrophic lateral sclerosis - Diagnosis, management 00:21:49

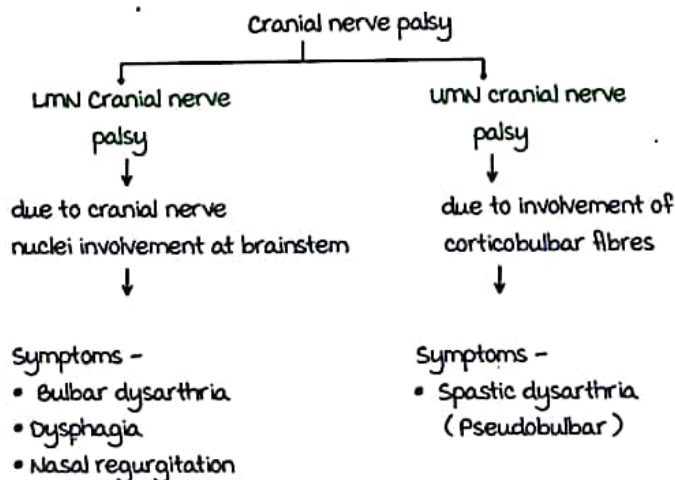


→ T₂ weighted MRI

shows hyperintensity within the corticospinal tract.

- Definitive diagnosis - Electromyography
Long duration polyphasic action potential is seen

Cranial nerve palsy in amyotrophic lateral sclerosis 00:45:07



- Flaccid tongue

- Palatal reflex
- Pharyngeal reflex
- Jaw Jerk
- Emotional incontinence
- Small, spastic tongue
- Painful yawning

CLINICAL FEATURE	PSEUDOBULBAR PALS	BULBAR PALS
PALATAL REFLEX	++++	—
PHARYNGEAL REFLEX	++++	—
JAW JERK	++++	—
EMOTIONAL	++++	—
PARALYSIS	SPASTIC	FLACCID
DYSARTHRIA	SPASTIC	FLACCID
TONGUE	SMALL, SPASTIC	WRINKLING/ATROPHIC/FASCICULATIONS



Split hand Syndrome

→
Thenar eminence
affected > Hypothenar

management

- Riluzole - reduces excitotoxicity by inhibiting glutamate release
- Edaravone - free radical scavenger

X-linked spinobulbar muscle atrophy

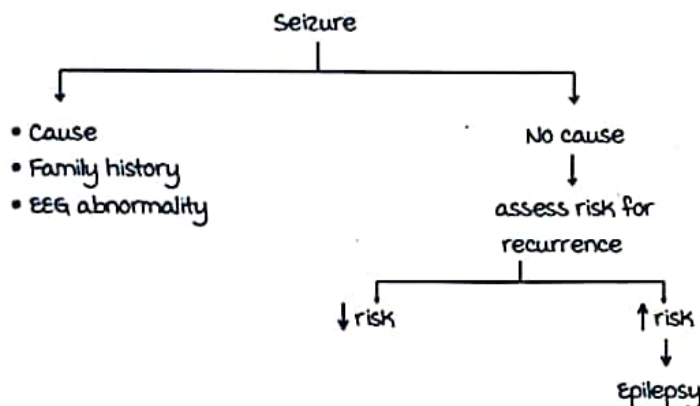
00:24:19

- A/K/A Kennedys disease
- Pure LMN type
- X-linked trinucleotide disease
- Associated with Androgen insensitivity
- Progressive weakness of limb and bulbar muscles

SEIZURES AND EPILEPSY- 1

Seizure - Paroxysmal, abnormal / excessive or hypersynchronous neuronal activity in the brain

Epilepsy - a or more unprovoked seizure without any identifiable cause leads to clinical syndrome called as epilepsy

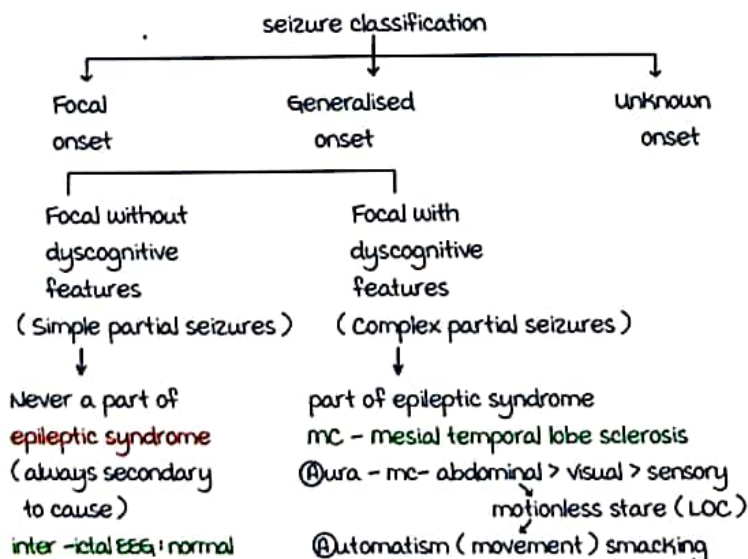


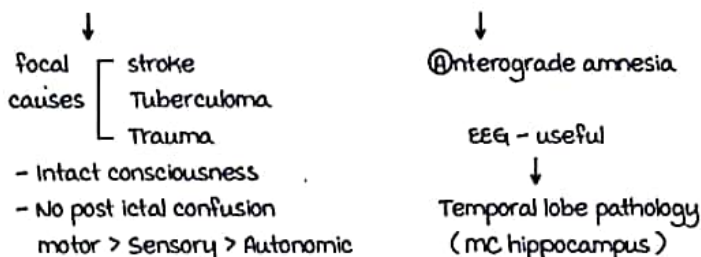
Classification of seizure

00:11:04

New definition suggests that one epileptic seizure is sufficient to term it as epilepsy if there is additional enduring alteration in brain that increases likelihood of seizures. Old classification -

- Generalised - Tonic clonic, absence, atonic, myoclonic
- Partial
 - simple → intact awareness (focal without dyscognition)
 - (focal) complex → loss of awareness (focal with dyscognition)





Simple partial seizure

00:21:26

1. Jacksonian march - distal → proximal, upper limb
2. Todd's palsy - post ictal transient weakness of upper limb > lower limb (12-24 hours)
3. Epilepsy Partialis continua - Continuous SPS which are lasting for > 24 hours

↓

Refractory to drugs (Rare)

jective → sensory / psychic phenomena

→ may be part of SPS

Aura can include paresthesias / flashing light / autonomic

Complex partial seizure

00:27:55

mesial temporal sclerosis

- T₂ MRI - Abnormal Hyperintensity + small sized asymmetrical hippocampus

↓

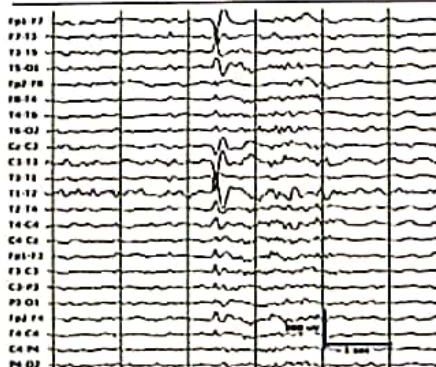
medically refractory seizures
Surgically treatable with hippocampectomy
H/o febrile seizure in childhood

↓

⊕ Post ictal disorientation

EEG in complex partial seizure

00:37:40



Spike

Sharp

Spike & wave

Sharp & wave

EEG - Focal (temporal) spikes / sharps

↓
Complex partial seizures

Generalised seizures:

- Absence
- Tonic clonic
- Atonic

Generalised - absence seizure

00:43:51

- Part of epileptiform syndrome
- Age of onset 6 years
- M > F
- Sudden brief LOC without loss of postural control

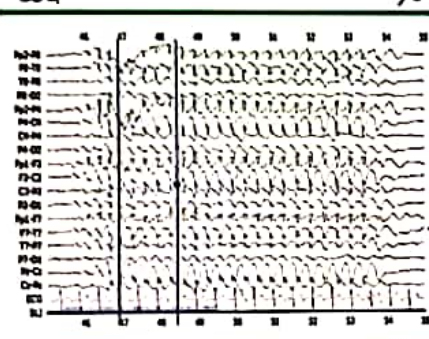
↓
Regains consciousness quickly

↓
No post ictal confusion

- Hyperventilation can precipitate the seizure
- Presentation - Day dreaming with normal IQ

mri - (N)

EEG -



Slow Spike and wave

poly Spikes & wave

∴ EEG - Generalised 3Hz slow spike and wave

Atypical absence seizure

00:52:16

- 1) LOC for longer duration
- 2) motor signs
- 3) Asymmetrical 3Hz spike and wave

↓
Abnormal inter-ictal back ground

Myoclonic seizure

00:53:47

- Sudden brief electric shock like contraction

↓
myoclonus

It can be subtle → dramatic

- LOC - impossible to determine
- Epileptic syndrome - juvenile myoclonic epilepsy
- Can be component of GTCS / absence
- Juvenile myoclonic epilepsy → upper limb > lower limb
- Adolescent
- IQ normal
- F > m
- Upon awakening
- Triggered by sleep deprivation
- Associated with GTCS / absence
- Respond to drugs → Lifetime valproate therapy
- Carbamazepine / phenytoin

↓ Trigger

myoclonic epilepsy / seizures

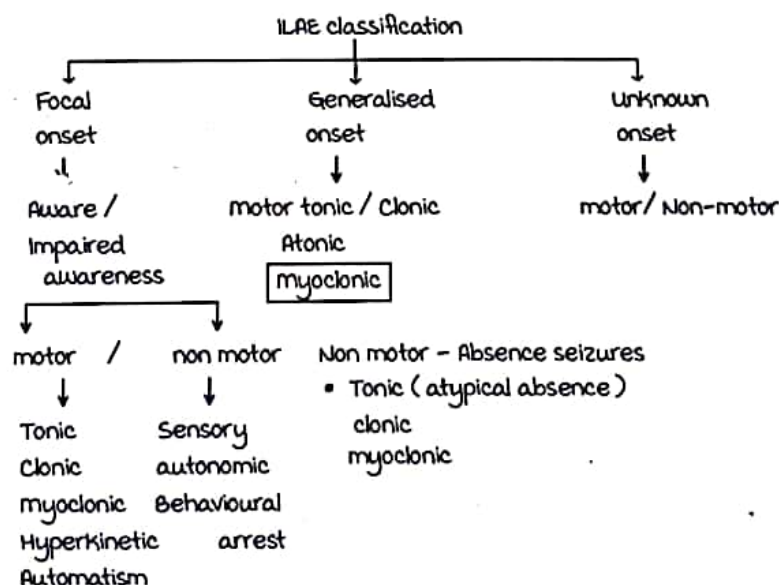
Levetiracetam
Lamotrigine
Topiramate } Rx

EEG - Generalised slow poly spike and wave

Atonic seizure

01:01:58

- Part of epileptic Syndromes
- Associated with myoclonic seizure
- Lennox gestaut syndrome
- Characterised by sudden loss of tone



SEIZURES AND EPILEPSY - 2

Seizures V/S Syncope

00:00:27

→ MC differential diagnosis of seizures is syncope

Types of syncope :

- (1) Vasovagal syncope (MC)
- (2) Cardiac syncope.
- (3) Orthostatic hypotension

Vasovagal syncope

- Unpleasant to patients, → prefers to lie flat.

Features .

- (1) Precipitating factor → emotional
- (2) Premonitory symptoms → Nausea, Sweating, Thirsty,
Feeling of warmth, tunneling
of vision
Appears pale
- (3) Position → erect
- (4) Gradual LOC with few myoclonic jerks.
- (5) Transition to LOC → gradual over seconds.
- (6) Regaining consciousness → rapid within seconds.
- (7) Post ictal period → No confusion / disorientation
(maximum < 5 mins)
- (8) Tonic clonic movements → may be present
(< 15 seconds)
- (9) Other features → Biting of tongue
(rare) Bladder / bowel incontinence .

TABLE 418-7 Features That Distinguish Generalized Tonic-Clonic Seizure from Syncope

FEATURES	SEIZURE	SYNCOPE
Immediate precipitating factors	Usually none	Emotional stress, Valsalva, orthostatic hypotension, cardiac etiologies
Premonitory symptoms	None or rare (e.g., odd odor)	Tiredness, nausea, diaphoresis, tunneling of vision
Posture at onset	Variable	Usually erect
Transition to unconsciousness	Often immediate	Gradual over seconds*
Duration of unconsciousness	Minutes	Seconds
Duration of tonic or clonic movements	30–60 s	Never > 15 s
Facial appearance during event	Cyanosis, frothing at mouth	Pallor
Disorientation and sleepiness after event	Many minutes to hours	< 5 min
Aching of muscles after event	Often	Sometimes
Biting of tongue	Sometimes	Rarely
Incontinence	Sometimes	Sometimes
Headache	Sometimes	Rarely

Active space

Pseudo seizures.

MC seen in adolescent age.

Features	Pseudo seizures	True seizures
(i) Axial thrusting movements	Present	Absent
(ii) Pupils	Normal	Dilated (Sympathetic Activity)

Generalized Tonic Clonic Seizures [GTCS]

00:07:52

- In generalised seizures



MC type : Tonic clonic seizures

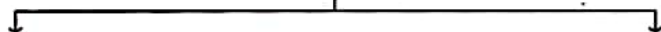


Called as GTCS.

Causes :

- (1) Epilepsy
 - (2) Medical cause.
 - (3) Non compliance with drugs → MC cause in India
- Status Epilepticus (SE)

Definition

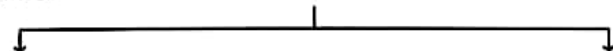


- 5 minutes or more of Continuous seizures
- Or
- 2 or more discrete Seizures without regaining Consciousness in between

Operational definition.

- 5 minutes or more of
- Continuous clinical and/or electrographic seizure Activity
- or
- Recurrent seizure Activity without recovery (Impairment to baseline) between seizures.

2 Phases



Initial compensatory phase.

- (1) ↑ Sympathetic activity
- lapse.
- (2) ↑ Cardiac output
- (3) ↑ Blood pressure.
- (4) ↑ RBS (sugar levels)

Decompensation phase.

- (1) Cardiorespiratory col-
- (2) Electrolyte imbalance.
- (3) Rhabdomyolysis and delayed tubular necrosis
- (4) Hyperthermia.

(5) ↑ Lactate level

(5) multi organ failure

(6) ↑ Intra cranial pressure
and cerebral edema

Diagnosis :

Continuous EEG monitoring .

- Initiated within 1 hour of seizure.
- Done for atleast 48 hours
- Evaluate for non-convulsive seizures.

Causes Of Seizures

00:14:20

① Drug associated (MC)



Non adherence to drugs (MC in India)

- (2) Alcohol (2nd MC) → intoxication / withdrawal.
- (3) Barbiturates, Benzodiazepines → intoxication / withdrawal.
- (4) Traumatic
- (5) Stroke/ tumor (mostly focal seizures)
- (6) Chronic structural injury to brain.
- (7) Metabolic causes.
 - Hypoglycaemia
 - Hypo / Hypernatremia
 - Hypocalcemia
 - Hypomagnesemia
 - Hypo/ Hyper Kalemia not related to seizures.
 - Hyper phosphatemia → seizures when associated with hypocalcemia
- (8) Hepatic encephalopathy.
- (9) Uremic encephalopathy.
- (10) Sepsis.

Drugs precipitating seizures

- Theophylline
- Imipenem
- Cefepime
- Quinolones
- Lithium
- TCA

Other causes :

- Viral encephalitis :
inc cause for new onset refractory status epilepticus (NORSE)
- Autoimmune encephalitis .
anti NMDA ab (N- methyl D- aspartate Ab)
- Paraneoplastic encephalitis - anti Yo Ab.

Management Of Status Epilepticus

00:20:56

Initial stabilization (2 IV lines)

- 1st IV line : Lorazepam (DOC) 0.1 mg / Kg (IV)
or
• midazolam 0.2 mg / Kg (IV / IM)
0.5 mg / Kg (buccal / intranasal)
or
• Clonazepam 0.015 mg / Kg IV

2nd line

- Phenytoin / Fosphenytoin 20 mg / Kg
or
• Levetiracetam 20-30 mg / Kg
or
• Valproate 20-30 mg / Kg

↓
15-20 minutes

No response

- IV Propofol ± midazolam

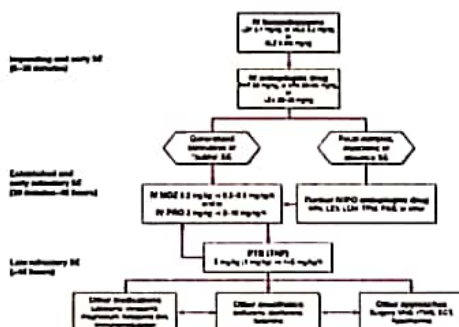
↓ No response

Refractory status epilepticus.

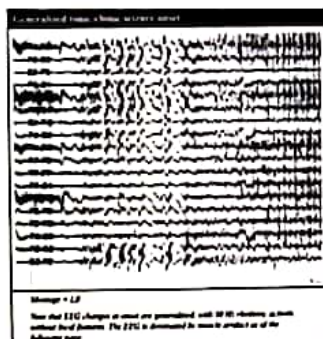
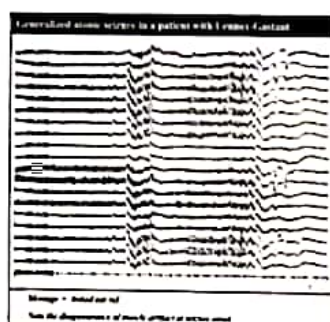
DOC : Phenobarbitone

↓ No response

Anesthetic drugs



EEG pattern



- In status epilepticus → generalised, poly spikes
- In focal
 - Simple partial seizures → normal EEG pattern
 - Complex partial seizures → regional spikes (temporal lobe)
- GTCS → poly spikes
- Atonic seizures CME → polyspikes and wave pattern
- Absent seizures → 3 Hz wave pattern and wave pattern

Management Of Generalised Seizures

00:27:47

Indication:

- 1st attack of seizure with high risk →
 - Post seizure EEG abnormality.
 - Family history of epilepsy.

(a) 2nd attack of epilepsy.

Drugs:

1st line

Valproate (DCC)

- 50-125 $\mu\text{g}/\text{ml}$
- Dose related toxicity:
 - Ataxia
 - Sedation
 - Tremors
- Inhibits metabolism of other drugs.
- Side effects:
 - Vomiting

Lamotrigine

- 2.5-20 $\mu\text{g}/\text{ml}$
- Dose dependent toxicity
 - Ataxia
 - Diplopia
 - Sedation
 - Steven Johnson Syndrome

Active space

- ↑ Ammonia levels
- Alopecia
- Liver toxicity
- Pancreatitis
- Renal side effects
- Weight gain
- Thrombocytopenia
- Teratogenic

2nd line drugs:

- (1) Carbamazepine
- (2) Topiramate → Renal stones
Weight loss
Glaucoma

- (3) Felbamate - Aplastic Anemia

- (4) Zonisamide - Renal stones

- (5) Phenytoin

- Indications to stop drugs:
2 year seizure free interval
with: (1) No family history
(2) Normal EEG
(3) Normal MRI

TABLE 10.10 SELECTION OF ANTIEPILEPTIC DRUGS

Generalized Onset Type: Clonus	Focal	Typical Absence	Atypical Absence, Myoclonus, Atonic
First-Line			
Lamotrigine	Lamotrigine	Valproic acid	Valproic acid
Valproic acid	Carbamazepine	Ethosuximide	Lamotrigine
	Chlorzoxazone	Lamotrigine	Topiramate
	Phenytoin		
	Levetiracetam		
Alternatives			
Zonisamide	Topiramate	Lamotrigine	Clobazam
Phenytoin	Zonisamide	Clobazam	Felbamate
Carbamazepine	Valproic acid		Clobazam
Chlorzoxazone	"Tegaserod"		Rufinamide
Topiramate	Clobazam		
Phenobarbital	Levetiracetam		
Phenacemide	Etosuximide		
Felbamate	Phenobarbital		
	Phenacemide		
	Felbamate		

*All drugs are AEDs

Management Of Absence Seizures And Partial Seizures 00:35:58

- Absence seizures.

1st line drugs

valproate (DOC)

Ethosuximide SE: Optic nerve damage

- Drugs in management of partial seizures:

- (1) Carbamazepine (DOC)

→ 4-12 µg/ml

→ Dose dependent toxicity

Ataxia

Diplopia

vertigo

→ Side effects:

SIADH

Liver toxicity

Aplastic anemia

2nd line drugs

Lamotrigine

Clobazepam

Active space

- (2) Levetiracetam
- (3) Phenytoin
- (4) Lamotrigine

→ management of seizures in pregnancy

• Drugs with →

- ① maximum risk for fetal malformation



valproate (4.7-10%)

- (a) least risk for fetal malformation

→ Lamotrigine (2-3.4%)

→ Levetiracetam (0 - 2.4%)

• Preferred drugs for seizures in pregnancy.

→ Lamotrigine (DOC)

→ Levetiracetam

• Folic acid given along with these drugs.

• 50-30-20 Rule.

50% → no change in status of seizures.

30% → seizure worsen / increase

20% → improvement of seizure

Laforas Disease And Rolandic Seizures

00:41:55

Laforas disease

→ aka progressive myoclonic epilepsy

→ Autosomal recessive

→ 10-18 years.

→ Poor prognosis

→ Clinical features.

- ① myoclonus

(a) Dementia

(3) Hallucination

(4) Low IQ

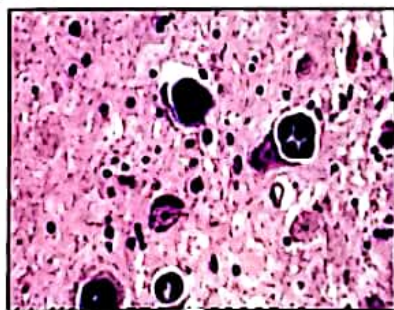
microscopy: PAS positive



Intracellular polyglucosan
inclusion bodies



"Lafora bodies"



Rolandic seizures.

→ 5-10 years of age

→ completely resolves by puberty.

→ good prognosis

→ aka : Benign epilepsy with centrotemporal high voltage spikes

→ Infrequent partial seizures .

West Syndrome

00:44:44

- aka infantile spasms
- age 3-7 months .
- boys > girls .
- In 2/3rd cases

↓
Structural brain lesion

↓
Due to brain hypoxia during delivery .

- Associated with tuberous sclerosis

- Clinical features :

- Triad of (1) Infantile spasm / jack knife / flexor spasm / salaam spasms (40%)
- (2) severe mental retardation
- (3) EEG - Hypsarrhythmia .
(large mountain waves)

- Psychomotor deterioration

- Permanent motor and mental disability

Salaam spasm

abrupt flexion of neck and trunk



arms raise forwards



flexion at elbow



legs elevated with flexion at hips and knees .

- EEG

Large mountain waves
(Himalayan waves)

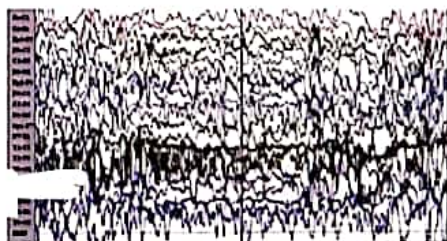
management

- ACTH

- Vigabatrin



- In case of tuberous sclerosis
- Visual field defects .



Lennox Gastaut Syndrome

00:48:17

- most severe childhood epilepsy
- bad prognosis
- progressive cognitive disturbance.
- Clinical features (triad)
 - (1) multiple types of seizure - mostly atonic
 - (2) severe mental retardation.
 - (3) Characteristic EEG.

EEG

- Slow spikes (1.5 - 2.5 Hz)
- Spike and wave pattern.
- bilaterally synchronous
- dominant over frontocentral region
- Symmetric.

management.

Lamotrigine + valproate

- Drug with :
 - Effect on cognitive function → Felbamate
 - Effect against drop attacks → Topiramate.
- Surgery : Callosotomy
- New drug : Cannabidiol

Syrnrome

- Refractory unremitting focal seizure in children
- Cerebral hemiatrophy
- Contralateral hemiparesis

EEG.

- Periodic lateralised epileptiform discharges.

Landau's perisylvian seizure

- Abrupt loss of previously acquired language at 5-7 years
- Epileptiform activity in perisylvian zone

Benign neonatal familial convulsions.

- 5th day seizures
- Due to potassium channel defect.

DEMYELINATING DISORDERS OF CNS

- myelin in CNS - By oligodendrocytes
- myelin in PNS - By Schwann cells
- Biochemical abnormality in myelin - Leukodystrophy

multiple sclerosis : [MS]

Antibodies + T - cells

Target Antigens : myelinoligodendrocyte glycoprotein (MOGP)
myelin Basic protein (MBP)

Loss of myelin sheath [Demyelination]

Loss of saltatory conduction

Continuous propagation of nerve impulse instead of
saltatory conduction → less effective

- T cell + Antibody mediated → Autoimmune demyelination

F >> M . [20 - 40 years]

- Chronic inflammation + demyelination → Gliosis / scarring

2° Axonal injury

Cerebral atrophy

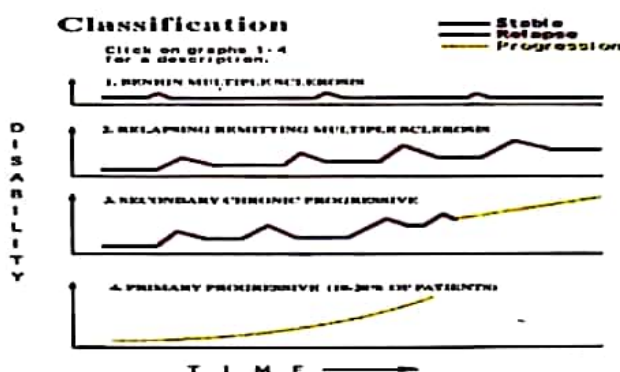
- MS is purely a CNS disease . No demyelination occurs in PNS .
- Perivascular cuffing :- by T-cell infiltrate

Affect white matter, disruption of BBB, demyelination and loss
of saltatory conduction

Active space

Classification Of M.S

00:07:34



Types : Relapsing remitting type - 85% - most common, good prognosis
 Primary progressive - 15% - Bad prognosis, and most common
 Secondary chronic progressive - Bad prognosis, rare

Benign MS - Best prognosis

Clinical Features :

- F >> M - 20-40 years
 - Associated with other autoimmune illnesses
 - 33% risk if identical twin has MS.
 - Vit D deficiency -
 - High socioeconomic status
 - Associated with HLA DRB1*1501
- HLA DR 2
- } Risk factors.

Cumulative Axonal loss is the cause for progressive neuronal damage MS.

Clinical Presentations :

- most common : Long tract symptoms - Sensory
- 2nd MC : Optic neuritis
- motor presentation - 3rd MC.
- Autonomic presentation - 4th MC.
- Spinal cord syndrome : presents as Acute Transverse myelitis
- Rarely - MC in PPMs (Primary Progressive MS)
- Brain stem syndrome

Long Tract Symptoms :

- Sensory > motor.
- Paresthesia / Hyperesthesia
- Unpleasant sensations are also common.
- Spasticity causing movement induced muscle spasms
- UMN type of weakness with loss of strength, Speed & exercise induced fatigue

Active space

Optic Neuritis :

- Painful monocular loss of vision .
- Optic Atrophy
- Fundus - Normal
- Diplopia - Binocular due to B/L INO (Internuclear Ophthalmoplegia).

Brain stem :

- Ataxia
- Tinnitus
- Vertigo

Rare :

- Bell's palsy with preserved taste .
- B/L Trigeminal neuralgia .
- Cognition is preserved till the end .
- Detrusor sphincter dyssynergia / detrusor hyperreflexia .
- Cognitive loss towards the late stage

Positive Symptoms Of MS :

1. Uhthoff's phenomenon : Abnormal Heat Sensitivity
Unilateral visual blurring in hot showers .
2. Lhermitte's sign : Not specific
Flexion of neck → Shock like sensation in back
3. Facial myokymia : Abnormal facial flickering
4. Glossopharyngeal Neuralgia

Diagnosis Of M.S

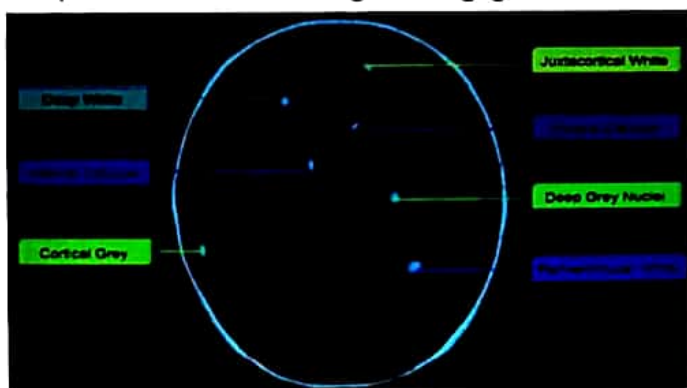
00:23:50

- mainstay : MRI

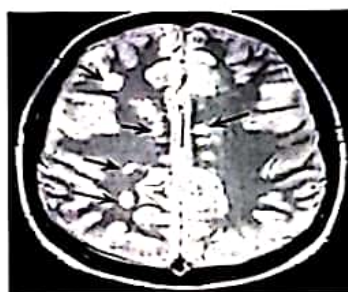


- Common sites for T_2 hyperintensities on T_2 w MRI :
- Juxtacortical -
- Periventricular - most common
- Internal capsule
- Deep white matter

- Brain stem - especially adjacent to CSF space.
- Cerebellum
- Spinal cord
- Corpus callosum - Dawson's fingers - Very typical



T2 W MRI



McDonald's criteria for MS:

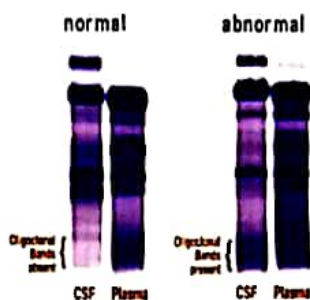
Mc Donald criteria for MS		
ATTACKS	LESIONS	ADDITIONAL CRITERIA FOR DIAGNOSIS MS
2 or more	2 or more	None. Clinical evidence alone will suffice
2 or more	1 lesion	Dissemination in space on MR (or await further clinical attack implicating a different CNS site)
1 attack	2 lesions	Dissemination in time on MR (or await further clinical attack implicating a different CNS site)
1 attack	1 lesion	Dissemination in space and time (or await further clinical attack implicating a different CNS site)
0 attack progression from onset		AND at least 2 out of 3 criteria: • Dissemination in space in the brain • Dissemination in space in the spinal cord based on 2 or more T2 lesions • Positive CSF

- Kurtzker's disability score - For MS.
- In CSF: Oligoclonal bands - Detected by Immunofixation electrophoresis

Intrathecal IgG

(Present in CSF & Absent in Serum)

- CSF pressure - Normal
- Cell - Increased in 1/3rd patients
- Proteins - ↑ IgG



Treatment of MS :

Disease course/stage

Monosymptomatic-Acute attack

*Relapsing-remitting
no disease activity
and/or no activity on MRI*

*Relapsing-remitting,
current disease activity
and/or activity on MRI*

Treatment options

IV methylprednisolone
1000 mg for 5 days,
without oral taper

IV corticosteroids
if acute attack occurs

IV corticosteroids for acute attacks,
plus for prevention
(1) INF β-1b, 30 µg IM weekly;

(2) Glatiramer, 20 µg SC daily

- Acute attack - IV methyl Prednisolone
- Disease modifying therapies :
 - IFNβ
 - Glatiramer acetate
 - Natalizumab
 - Fingolimod
 - mitoxantrone

Neuromyelitis optica / Devic's disease

00:36:43

- Acquired disease
- Auto-antibodies against Aquaporin 4
- Autoimmune, MC IN females - 40%
- Severe transverse myelitis + B/L Acute optic neuritis
- Disabling disease, Non progressive

Treatment : Responsive to steroids

↓ fails
plasma exchange (PLEX)

- Normal MRI

Acute Disseminated Encephalomyelitis (ADEM)

00:39:40

Definition : Acute inflammatory Demyelinating disorder of CNS, characterised by multifocal white matter involvement which is typically monophasic and usually follows an infection or vaccination .

- Post infectious - 95%
- 5% follow immunisation
- Children > Adults
- most common cause : Rubella > measles > chicken pox
- Reason : molecular mimicry
- Clinical Presentation :
 - Prodromal symptoms - 20%
 - Meningismus
 - Encephalopathy
 - Coma
 - B/L Extensor plantar.
 - Very Rapid progression .
- In CSF : Oligoclonal bands ; Pleocytosis.
- On MRI : Asymmetrical large Hyperintensities on T₂W MRI
- Treatment : Steroids +/- PLEX.

Difference between MS and ADEM

ADEM

- Age: before 12 yrs
- Male preponderance in children; reversed in adults
- Preceding triggers.
- Constitutional symptoms

MS

- Age: After 12 yrs.
- twice common in women
- No preceding triggers.
- No constitutional symptoms

ADEM

- ON - Bilateral
- Complete myelopathy - unusual
- Encephalopathy - common
- Monophasic

MS

- ON-unilateral
- Myelopathy - complete
- Encephalopathy -less common
- Relapsing remitting

CORTEX - LOBAR ORGANISATION - I

Neurological examination :

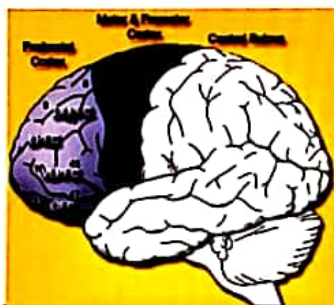
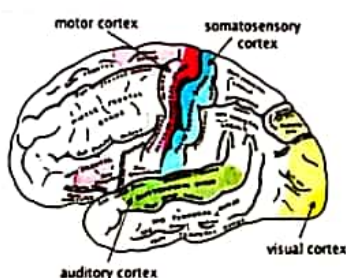
- I. Higher mental functions
 - II. Cranial nerves
 - III. motor system examination
 - IV. Sensory system examination
 - V. Cerebellum
 - VI. Miscellaneous - Autonomic nervous system
- meningeal signs
- Skull and spine

Frontal lobe - Motor area

00: 01:46

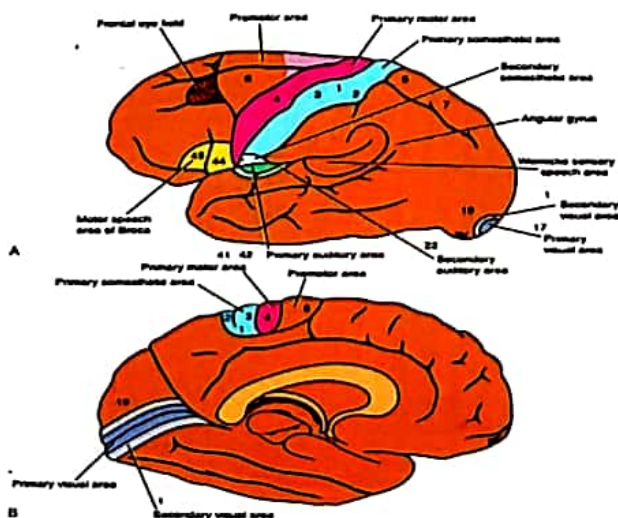
Organization of cortex :

Lobes - Frontal, Parietal, Temporal, Occipital



Superolateral surface :

Frontal lobe : lies above sylvian fissure and to the left of central



Active space

1. motor cortex (Area 4)

- precentral gyrus (location)
- Origin of 30% of corticospinal tract
- Lowest threshold to initiate movements
- Fine distal movements

Lesion of motor cortex:

involves middle cerebral artery

causes contralateral UMN weakness – predominantly face & arms

C/L simple partial seizures – marching / Jacksonian type.

↳ also called adverse seizures

Somatotropic representation →

Face & arms: represented on

Superolateral surface

Lower limbs: medial surface

(Supplied by anterior cerebral artery)



Note:

motor cortex matures by age of 4 years

Betz cells: giant pyramidal cells in layer 5 of motor cortex

Frontal lobe - Premotor cortex

00:10:36

- also called supplementary motor cortex.
- Pre-motor cortex: Area 6, 8
- origin of 30% of cortico-spinal tract
- function: Planning and organizing sequence of movements.

Lesion of pre-motor cortex:

- Spasticity more than weakness.
- Primitive reflexes ⊕

Frontal eye field

00:15:45

- anterior to pre-motor cortex
- part of pre-frontal cortex (area 9, 10, 11)

Function:

helps to look to opposite side

i.e.: ① frontal eye field → activate ② VI nerve nucleus

② Lateral rectus

Look to right side

Lesion of frontal eye field:

Gaze towards site of lesion and away from side of weakness.

Eg: (L) UMN weakness → (R) frontal cortex lesion

(hemiplegia)

(R) frontal eye field affected.

Patient looks to

(R) side

Gaze towards site
of lesion

Cannot look to (L) side.

Gaze away from side of
weakness

Broca's area

00:20:58

Location: Inferior frontal gyrus

Area 44, 45

Lesion: Broca's aphasia

motor non-fluent aphasia

Word output ↓

Talks with difficulty

Dysarthric / Telegraphic speech

Prosody of speech → Lost

Pronunciation wrong

Comprehension intact

Repetition lost.

Pre-frontal cortex

00:24:20

Area 9, 10, 11

Functions → Personality

Problem solving ability and creativity

Intelligence

Executive function

Motivation

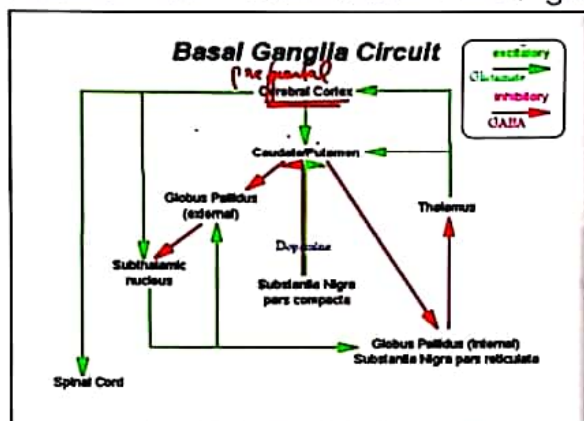
Abstract thinking

Attention
 Retrieval of memory
 Appropriate social behaviour
 Language.

Pick's disease : Atrophy of pre - frontal cortex .

Pre-frontal cortex connected to sub-cortex (striatum) by fronto striatal fibres .

∴ Pick's disease → motor manifestations like akinesia, rigidity



Frontal lobe - Medial surface

00:29:04

Predominant blood supply



Anterior cerebral artery (ACA)

Lesion in medial surface

Weakness in lower limbs

Urinary incontinence (Paracentral
 lobule involvement)



Cingulate gyrus : Emotional and conditional response .

Ex/In ACC.

causes $\rightarrow$ anterior Cingulate gyrus syndrome
 aka Akinetic mutism or Abulia



no movement (even to pain)
 no speech

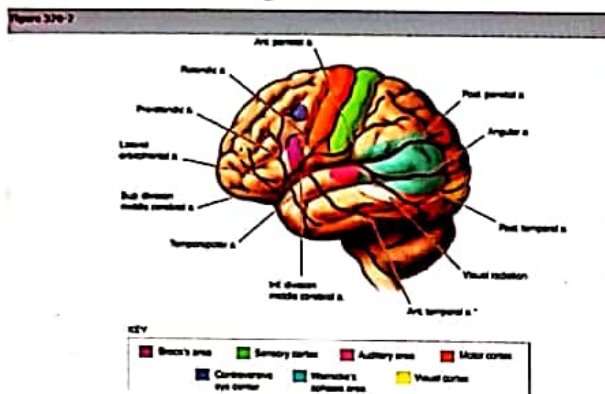
B / L frontal lobe lesions :

Akinetic mutism

Urinary incontinence

irreversible personality changes

Gait apraxia → K. a. Ignition Foot Phenomenon.



Parietal lobe

00:34:19

lies posterior to the central sulcus.

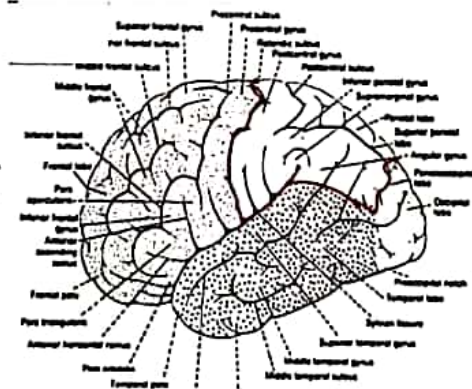
Boundaries :

Central sulcus

Sylvian fissure

Parieto - temporal sulcus

Parieto - occipital Sulcus



Parts of parietal cortex

1. Sensory cortex - Area 3, 1, 2

a) origin of 40 % of corticospinal tract

b) Sensations relayed to area 3, 1, 2.

- Cortical sensations



Tactile localization

Tactile / 2-point discrimination

Stereognosis

Graphesthesia

∴ Lesion of sensory cortex : C / L weakness
loss of cortical sensations .

2. Supramarginal gyrus

Function : Praxis .

Lesion :

Apraxia - Inability to carry out a voluntary motor act in the presence of normal motor / sensory system / cerebellum .

Types → Ideational apraxia
Ideomotor apraxia

3. Angular gyrus

Function : Enosis → Ability to recognize an object by touch or vision or sound .

Lesion of dominant lobe	a) Tactile agnosia (astereognosis) b) Acalculia c) Finger agnosia d) Right left disorientation e) Agraphia with alexia	Gerstmann Syndrome .
-------------------------	--	----------------------

Note :

Lesion of parietal lobe → Inferior homonymous quadrantanopia.

Non - dominant parietal lobe lesion

00:47:08

Features :

1. Visuo- Spatial disorientation
2. Constructional apraxia
3. Dressing apraxia
4. Anosognosia (Left sided hemispatial neglect)

right hemisphere → right & left extrapersonal space

left hemisphere → right extrapersonal space .

- when left hemisphere affected, right hemisphere compensates for right extrapersonal space
- when right hemisphere affected

No compensation .

∴ Left sided hemispatial neglect .

CORTEX - LOBAR ORGANISATION - 2

Temporal cortex

00:00:10

No Corticospinal tracts, $\therefore$ no weakness

Non - dominant hemisphere features ⊖

No sensory symptoms

Important areas :

1. Auditory cortex (area 41, 42)

↳ B/L lesion → deafness

Secondary auditory cortex

Lesion → auditory agnosia

2. Visual association cortex (area 20, 21)

Lesion → Visual agnosia

Other features of temporal lobe lesions :

- Superior homonymous quadrantanopia
- Olfactory and gustatory hallucinations

Wernicke's area :

Area 22 - in superior temporal gyrus

Lesion → Wernicke's aphasia [without weakness]

Fluent (sensory) aphasia .

Word output ↑↑

Jargon , neologism .

Comprehension and repetition - lost

Hippocampus :

Storage of short term memory

transfer of memory to neo cortex [for long term memory]

Lesion → Episodic ~~memory~~ ~~loss~~

Active space

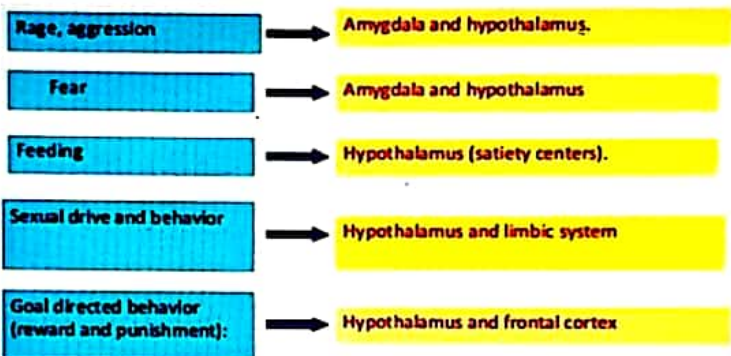
Amygdala

00:07:16

Amygdala (Limbic cortex)

B/L Lesion → Kluver Bucy syndrome

- ↑ Aggression
- Loss of fear
- loss of satiety
- ↑ Sexual drive
- Goal directed behaviour – lost



B/L Temporal lobe lesion

- 1) Kluver Bucy syndrome
- 2) Deafness
- 3) Korsakoff's amnesic state

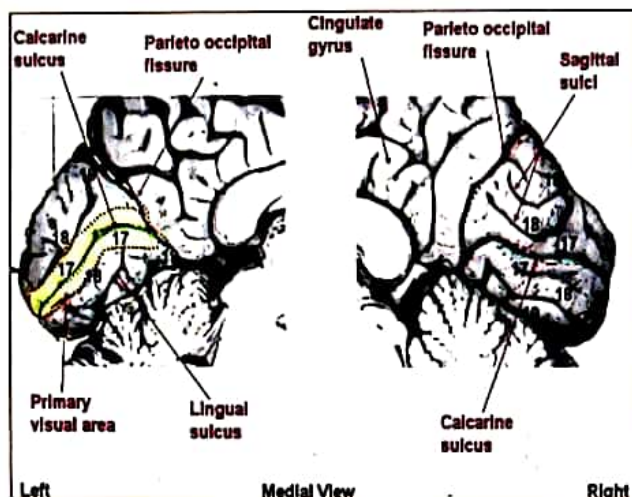
Occipital lobe

00:09:08

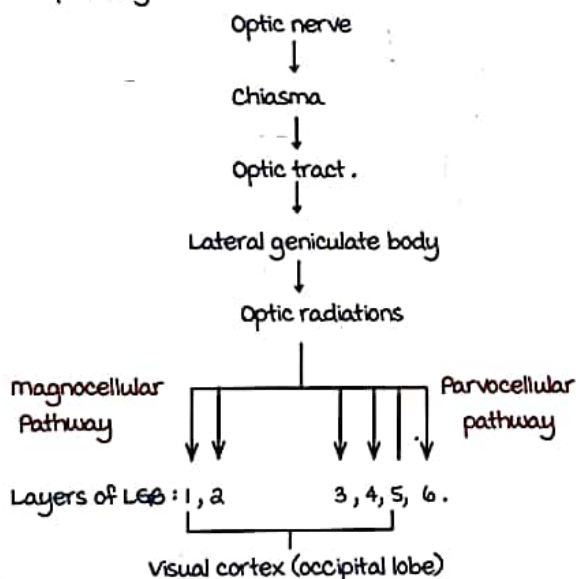
Primary visual cortex (area 17)

Secondary visual cortex

- Peristriate and parastriate cortex (area 18 / 19)
- function: visual memory
- ocular fixation.
- identify size / shape / colour



Visual pathway



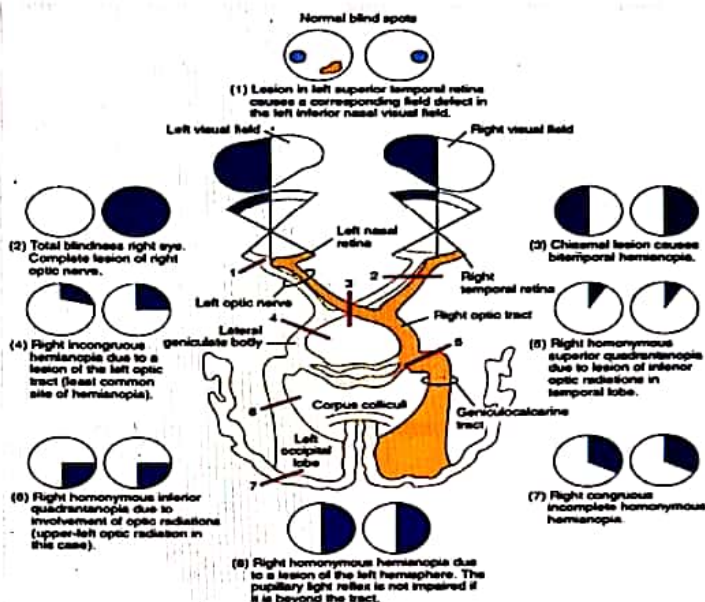
- Parvocellular pathway :
 - Smaller receptive field
 - Colour vision
 - No response to moving stimuli
 - Stereopsis / depth of vision

Lesions in visual pathway :

- Optic nerve → monocular vision loss
- Optic chiasma → Bi temporal (heteronymous) hemianopia
- Optic tract → Homonymous hemianopia (incongruous)
- Lateral Geniculate Body → Homonymous hemianopia

Optic radiations

- Temporal lobe : superior quadrantanopia
- Parietal lobe : inferior quadrantanopia



Visual Cortex Lesions

00:15:02

U/L lesion in visual cortex

- Contralateral homonymous hemianopia
- macular sparing +
- Congruous hemianopia

B/L visual cortex lesion :

Anton's syndrome

- Cortical blindness
- patient denies of blindness
- Light reflex preserved

Balint's syndrome

- Optic ataxia
- Oculomotor apraxia
- Simultagnosia

Agnosia in occipital lobe lesions :

- Colour agnosia
- Prosopagnosia [inability to identify person by face]

LOBAR DYSFUNCTION - APHASIA

Aphasia

- Disorder of language
- Dominant hemisphere lesion (cause)

Speech apparatus

Wernicke's area (area 22 in superior temporal gyrus)

Identifies word as a language symbol



Language symbols to be recognised



Sent to the angular gyrus



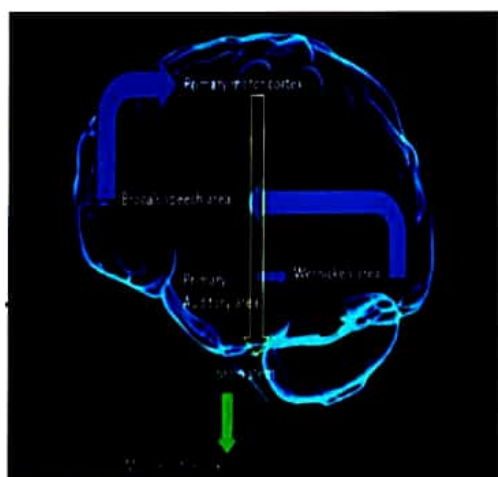
Sent back to Wernicke's area



sent to Broca's area by arcuate fasciculus
(area 44/45 - in inferior frontal gyrus)

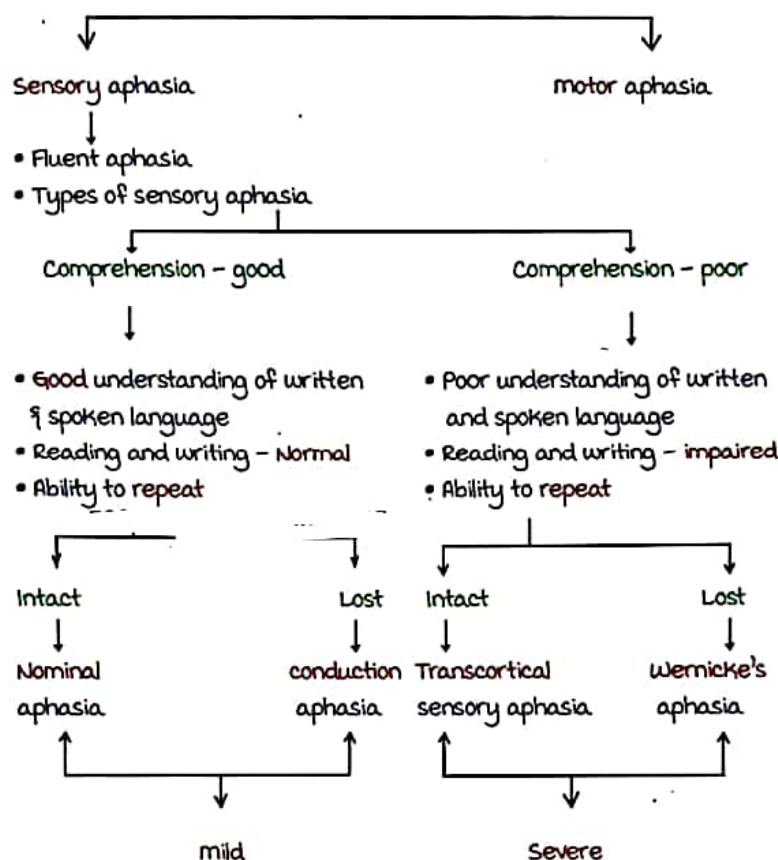


converts language symbol to motor activity



Aphasia - classification

00:05:38



Sensory aphasia - nominal and conduction aphasia

00:10:43

Nominal aphasia

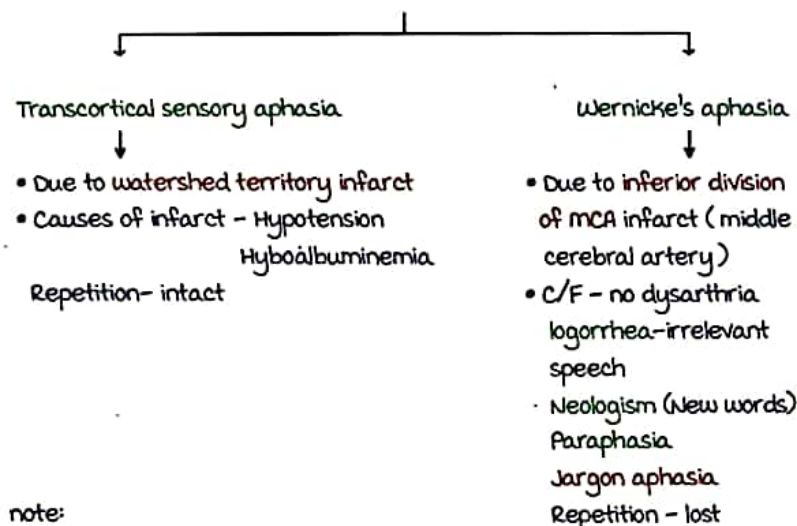
- Site of lesion - angular gyrus
- C/F: Difficulty in word finding or naming
Comprehension (+)
Repetition (+)
Good reading and writing skills
Good speech output

Conduction aphasia

- 1) Site of lesion - arcuate fasciculus
- 2) Repetition lost
- 3) Paraphasia (unintended words in between speech)

Sensory aphasia - Transcortical sensory , Wernicke's aphasia

00:15:07



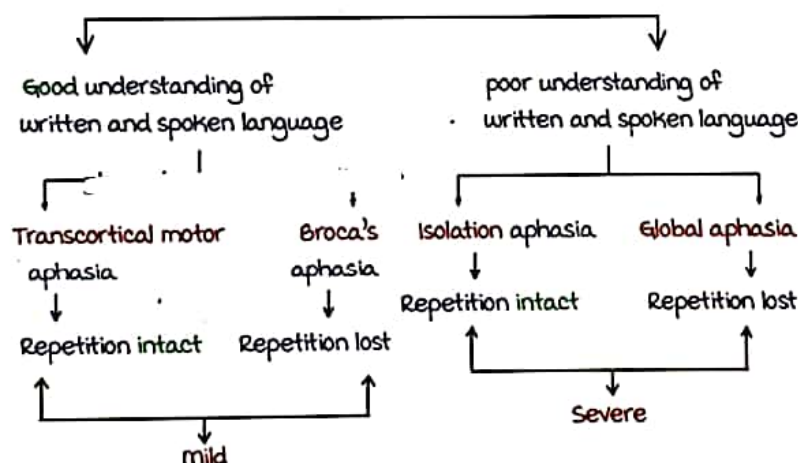
note:

common C/F (in both):

- loss of ability to understand written / spoken language
- impaired reading / writing

Motor aphasia

00:19:54



Broca's aphasia

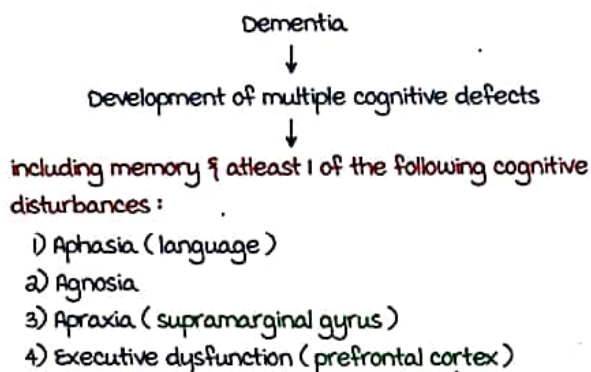
- Non fluent
- Dysarthria word finding difficulty
- Agrammatic, telegraphic speech
- Word output poor
- Prosody (rhythm) lost
- Pronunciation poor
- Impaired reading and writing

Active space

Broca Aphasia

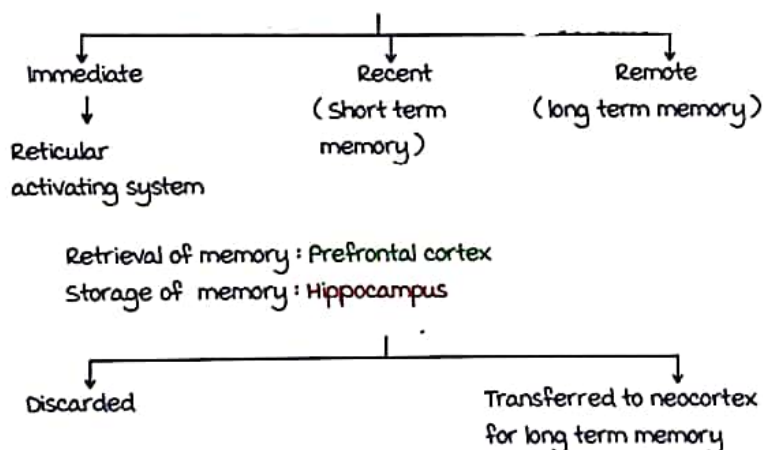
Feature	Syndrome
Spontaneous speech	Nonfluent, mute or telegraphic, usually dysarthric
Naming	Impaired
Comprehension	Intact (mild difficulty with complex grammatical phrases)
Repetition	Impaired
Reading	Often impaired ("third alexia")
Writing	Impaired (dysmorphic, dysgrammatical)
Associated signs	Right hemiparesis Right hemisensory loss ± Apraxia of left limbs

LOBAR DYSFUNCTION - DEMENTIA



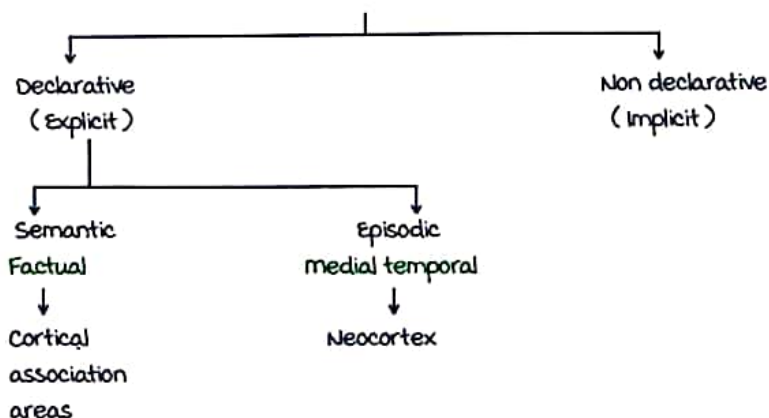
Memory

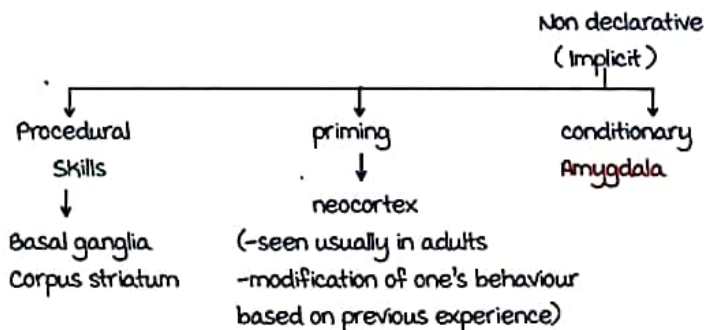
00:04:00



Long term memory

00:16:09



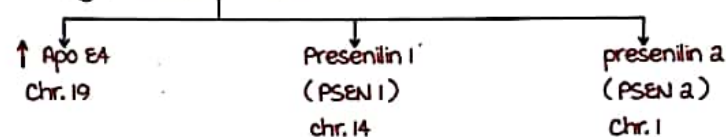


Dementia

00:26:47

Alzheimer's disease

- Biggest risk factor : Age
- < 65 years, Genetic factors



Critical molecule - $A\beta$ amyloid

{derived from APP gene

(amyloid precursor protein) on chr 21 }

- forms β pleated sheets that aggregates
- Resistant to degradation
- Neurotoxic response from astrocytes and microglia

Facts :

- most important genetic risk factor for sporadic - early alzheimer's disease
 - Single most important biological marker for AD risk
- Presenilin-1 (chr 14)
 - most common defect in early onset familial AD
 - involved in cleavage of APP
 - Presenilin-2 (chr 1)

Histopathology in Alzheimer's

00:34:15

Neurofibrillary
Hyperphosphorylated
Tau Protein
↓
Hence Known as Tauopathy

Neuritic plaques
A β amyloid



Risk factors

1. Old age
2. Positive family history
3. F $\times$ m
4. Aluminium / mercury
5. Apo E4 $\uparrow$ risk
6. History of head trauma & concussions
7. Past history of stroke

Alzheimer's disease = T₂DM

due to manifestation of insulin resistance in the brain

- Apo E4 / NSAIDS / HRT - protective factors

Pathology of Alzheimer's Disease

00:40:35

- 1) Hippocampus $\rightarrow$ Diffuse atrophy
- 2) Degeneration of cholinergic neurons of Nucleus basalis of Meynert.
- 3) Hyperphosphorylated tau protein - Neurofibrillary tangles
- 4) Senile / neuritic plaques - A β amyloid
- 5) Granulovacuolar degeneration

Clinical manifestations

-characteristic pattern of Alzheimer's-

memory impairment $\rightarrow$ language $\rightarrow$ Visuospatial defects $\rightarrow$ executive dysfunction

Stage of Alzheimer's disease

i Korsakoff's amnesic state

- 1) Hippocampal atrophy
- 2) Gradual onset of memory loss
- 3) Declarative episodic memory.

ii

- 1) dysnomia $\rightarrow$ affects language
 - nominal aphasia
 - comprehension
 - fluency
- 2) halting in speech / writing
- 3) Acalculia

iii) Visuospatial defects

Parietal 1) Praxia → Supramarginal gyrus

2) Gnosia → Angular gyrus

3) Non dominant → Visuospatial disorientation

• Constructional apraxia

• Anosognosia

iv) Prefrontal cortex - Personality affected

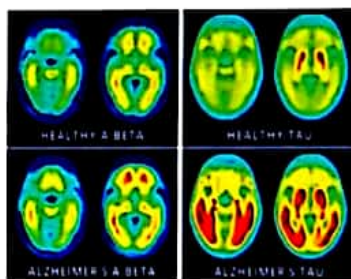
Alzheimer's - diagnosis

00:48:20

A PET Scan - IOC (earlier MRI was considered IOC)



- Hypometabolism
- Fibrillary A β amyloid
- hyperphosphorylated tau protein



B. EEG - normal or non specific slowing

C. CSF analysis

1) Low A β 42 amyloid levels

2) High phosphorylated tau levels

Differential diagnosis of alzheimer's

00:50:16

Differential diagnosis

- Pick's disease
- Vascular dementia
- Normal pressure hydrocephalus
- Diffuse Lewy body dementia

Reversible causes - Vitamin B12

- Thiamine

Treatment of Alzheimer's

Cholinesterase inhibitors are Doc

- Tacrine (hepatotoxic)
- Rivastigmine
- Donepezil (mc)
- Galantamine

moderate to severe : NMDA antagonist : memantine

Pick's disease (fronto-temporal dementia)

1. Age 50 - 70 yrs
2. Gene MAPT (Chr. 17)
3. 50% have family history
4. Hypophosphorylated tau protein
5. Pick's bodies



Contain hypophosphorylated tau

6. Selective atrophy of frontal and temporal

Disease starts in frontal (prefrontal cortex)



Behaviour & personality affected

MC variant - behavioural variant of Fronto temporal dementia (bvFTD)

7. +/- subcortical symptoms (reason - prefrontal cortex connected to corpus striatum)
 8. Impaired planning, judgement & language
- memory relatively preserved (in early stage)
 - Transcortical motor aphasia
 - Progresses rapidly.

DLB Dementia

UU:38:44

Cortical dementia	Subcortical dementia
1. Alzheimer's disease - Pick's disease 2. memory affected 3. more - severe 4. mood variations - rare 5. Extra pyramidal (-) 6. Aphasia	1. Huntington's disease - DLB dementia 2. memory - spared / less severe 3. Less severe 4. Common (Apathy, depression) 5. + 6. -
Apraxia Agnosia +	affects thalamus / corpus striatum / midbrain

Parkinson's Dementia

01:02:50

Parkinson's Dementia v/s DLB dementia

1) PD - unresponsive to L- dopa

Tremor uncommon

Cognitive impairment within 12 months of onset

2) Hallucination

3) B/L motor symptoms common

4) Axial symptoms / gait dysfunction - Early

NOTE:

- and MC cause of dementia - vascular dementia

- dementia can precede or occur along with parkinson's

- Never give antipsychoti-



↑ dopamine

- Dopaminergic deficit

α- synucleinopathies

- DLB dementia is an alpha synucleinopathy

- Intraneuronal cytoplasmic inclusions (ie lewy bodies) are seen in Substantia nigra, brainstem, limbic cortex

Prion disease

01:08:40

• Infectious proteins which lacks nucleic acid

- abnormal folding of prion protein [PrP]

normal- PrP

Abnormal- Prp → PrPsc

(alpha) (beta pleated)

- may manifest as : infectious/genetic/sporadic

- no immune response

- spongiform changes in cortex → neuronal loss

Example

1. Creutzfeldt - jakob disease

2. Gerstmann- straussler scheinker syndrome

3. Kuru

4. Familial fatal insomnia

- Diagnosis:
- 1) Long incubation period
 - 2) Dementia + myoclonus
 - 3) Ribbon shaped hyperintensities on MRI
 - 4) EEG - high voltage slow & sharp waves in a low voltage background



- IOC - Brain biopsy
 Drug - Flupirtine maleate
 (Centrally acting non opioid analgesic)

Vascular Dementia

01:15:04

- 2nd mc type of dementia
- Dementia - ~~vascular~~ cerebrovascular accident (CVA)
 - ↓ (Onset within 3 months of CVA)
 - Deterioration of cognitive function
- 1. Step wise deterioration
- 2. Prefrontal cortex
 - ↓
 - Executive function
 - ↓
 - Frontal
 - ↓
 - Parietal
- 3. B / L corticospinal & corticobulbar involvement
 - ↓
 - Appear like pseudobulbar palsy (Emotional Incontinence)
- 4. memory - involved later
- 5. urinary abnormalities
 - ↓
 - due to paracentral lobule involvement
- 6. Gait abnormality
 - ↓
 - Gait apraxia (Ignition foot abnormality)

7. Multiple lacunar infarcts (white matter disease)



Binswanger disease



Confusion + Psychosis + motor disability
MRI - Normal pressure hydrocephalus

D/O of dementia

- normal pressure hydrocephalus
- ventricles are filled with CSF & therefore expands the ventricle
- CSF pressure : normal
- cortical atrophy
- prominent sulci & gyri

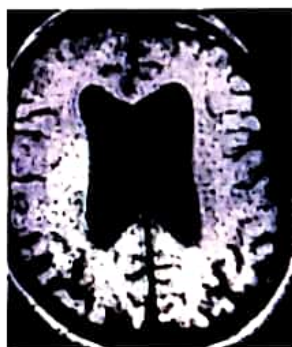
Triad

Dementia (Subcortical)

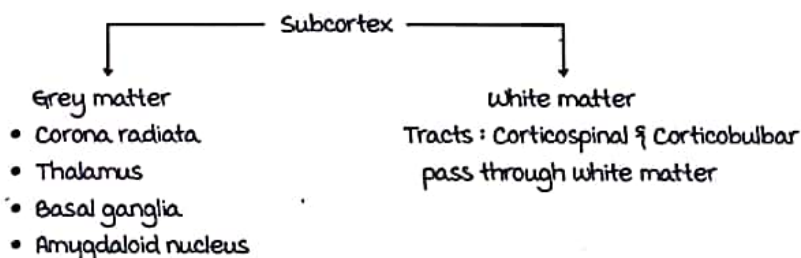
Ataxia

Urinary incontinence

"Gait apraxia" Ignition foot phenomenon



EPS : ANATOMY AND PHYSIOLOGY



Basal ganglia

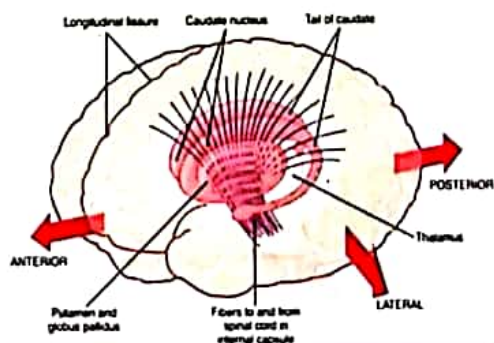
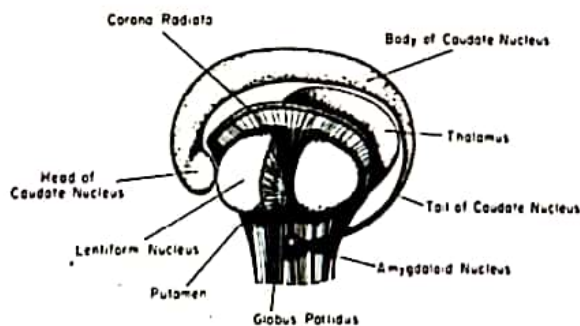
00:02:36

- Functionally related nuclei in the Subcortex :

- Caudate nucleus
- Putamen
- Globus pallidus
- Subthalamic nucleus
- Substantia nigra

} corpus striatum
} Lentiform nucleus

- All these nuclei form the largest component of EPS [Extra Pyramidal System]



Active space

EPS - components & basic functions

00:06:03

Components of EPS :

1. Basal ganglia with its connections
2. Rubrospinal tract (mid brain-red nucleus)
3. Reticulo spinal tract
4. Tecto spinal (tectal nuclei) tract
5. Vestibulo spinal tract

- These tracts do not cross through Pyramids of Thalamus. Hence called as EPS.
- Initiation & partly integration of fine, skilled distal voluntary movements controlled by Pyramidal tracts.
- prepares for movement, thought process, regulation of posture, modulation by EPS.
- Finesse to the movement - Cerebellum

Basic functions of EPS :

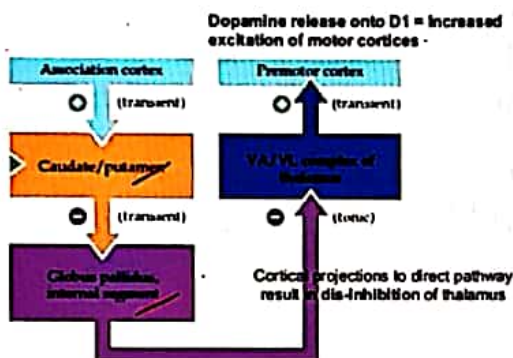
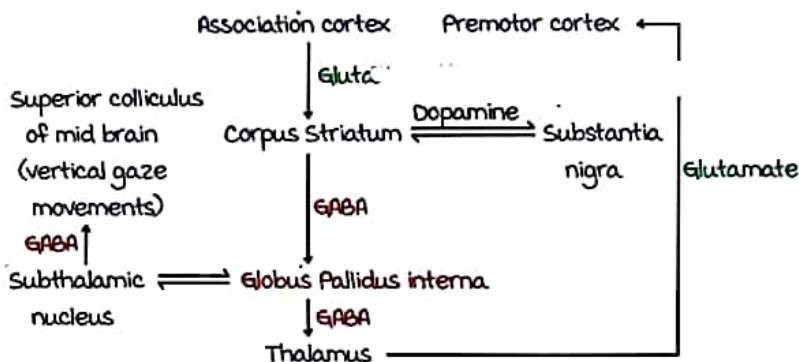
- Cognitive control of motor activity - Caudate nucleus
 - Complex patterns of motor activity
 - Timing and scaling the intensity of movements
- } EPS

Basal ganglia circuits

00:16:06

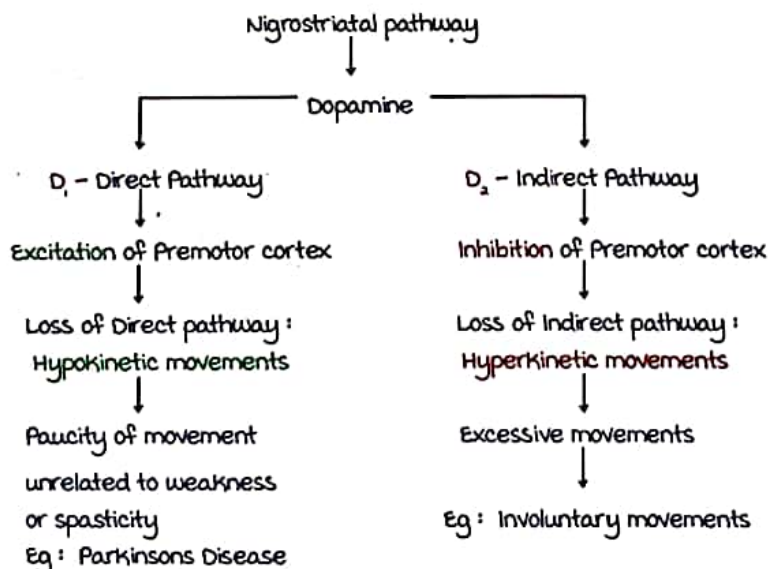
- Basal ganglia - Receives inputs from and projects back to motor cortex via thalamus
- It is a closed loop
- majority of the inputs to Basal ganglia
 - Corpus Striatum via Cortical Association areas
- main output of Basal ganglia
 - via Globus Pallidus interna > Substantia nigra
- Excitatory pathways - Glutamate
- Inhibitory pathways - GABA
- Dopaminergic pathways can be excitatory or inhibitory

Circuit :

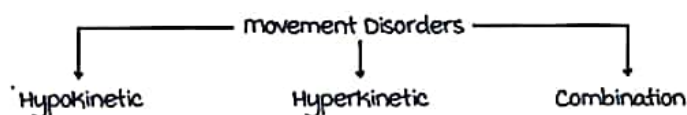


Direct and indirect pathways

00:30:35



Active space

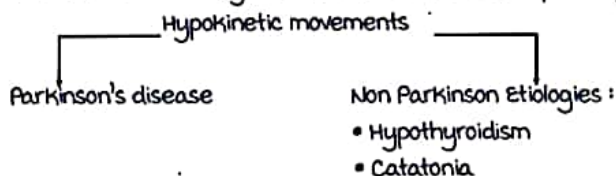


Basal ganglia summary :

- Planning, Programming and initiation of motor activity.
- Lesion : leads to alteration in the sum of impulses channelled to basal ganglia resulting in movement disorders.
- Crude movements also affected.

PARKINSON'S DISEASE

Hypokinetic movements : Paucity unrelated to weakness or spasticity



- most common Neurodegenerative disease : Alzheimer's disease
- 2nd most common Neurodegenerative Disease : Parkinson's disease
- most common Subcortical Neurodegenerative disease : Parkinson's disease .

Pathology :

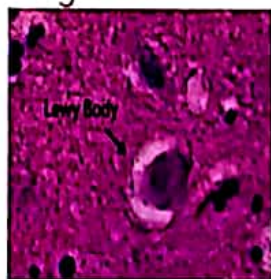
Subcortex → Grey matter → Basal ganglia

Nigrostriatal Dopaminergic Neurons gets degenerated.
[Direct pathway]

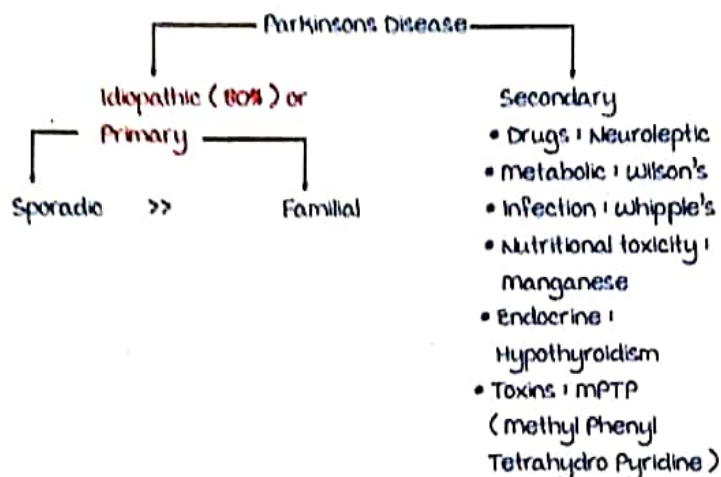
↓
Loss of excitatory signals to Premotor cortex

↓
Hypokinesia / Bradykinesia

- Age group of Parkinson's disease - 65 years and above.
- Less than 60 years - Familial Parkinson's disease
- Familial Parkinsons Disease
 - PARK 1 - AD - α - Synuclein - chr4
 - PARK 2 - AR - Parkin - chr6
- Intracytoplasmic proteinaceous inclusions called Lewy bodies
- On MRI : Loss of Pigmentation in Substantia nigra
 - MRI at the upper mid brain Shows B / L Hyperintense Grey matter (Substantia nigra.)
 - Absent Swallow tail Sign -
 - > 90 % Diagnostic accuracy



- Apart from Substantia nigra, Lewy bodies are also seen in
 - Other Pigmented Brain stem nuclei
 - Dorsal Nucleus of Vagus
 - Nucleus basalis
 - Other cortical association areas

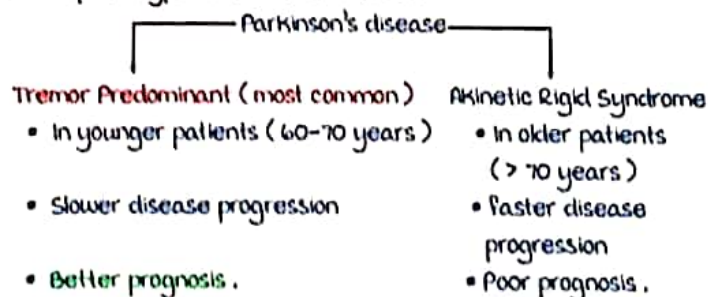


Symptomatology of Parkinson's disease

00:11:20

- Asymmetrical
 - Rigidity
 - Tremor
 - **Bradykinesia**
 - Postural instability

Clinical phenotypes of Parkinson's disease :



Tremor :

- the presenting Symptom.
- 2/3rd of the patients present with tremor.
- Asymmetrical
- Resting distal upper limb tremor

- Frequency : 4-6 Hz
- Brought on by concentration
- Pill-rolling tremor
- Pattern : Ipsilateral arm → Ipsilateral leg → Contralateral leg → Contralateral arm .

Characteristics	Parkinson's Disease Tremor	Essential Tremor
Tremor	At rest & reemergent tremor	Postural tremor
Frequency	4-6 Hz	5-12 Hz
Distribution	Asymmetric	Mostly symmetric
Body parts affected	Hands & legs	Hands, head, voice
Writing	Small (micrographia)	Large and tremulous
Course	Progressive	Stable or slowly progressive
Family history	Uncommon (1%)	Common (>30%)
Extrapyramidal signs (bradykinesia, rigidity, and loss of postural reflex)	Present	Absent
Relieving factors	Levodopa, dopamine agonists, anticholinergics	Alcohol, propranolol, primidone, topiramate, gabapentin, clonazepam
Usual site for surgical treatment with deep brain stimulation	Subthalamic nucleus or globus pallidus interna	Ventral intermediate thalamus

Bradykinesia :

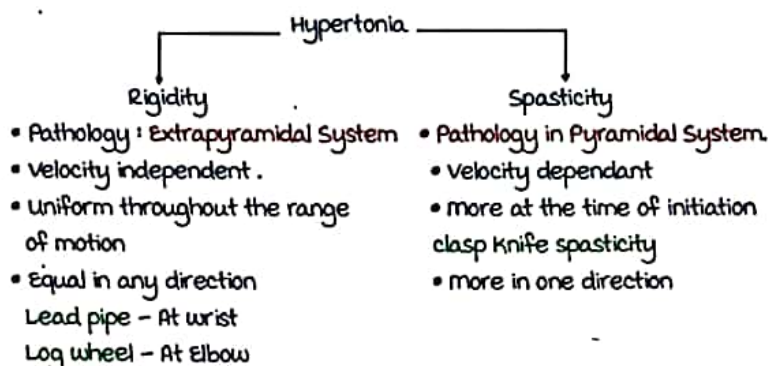
- Facial Hypomimia
- Reduced Arm swing
- Small Hand writing - micrographia
- Difficulty in fine limb movements - cutting , using zipper , Putting buttons .
- Wheel chair Sign : Rising from wheel chair
- Difficulty in turning in bed .
- Hypophonic voice
- Stooped Posture
- Bradykinesia + Posture instability →
 - Poor balance
 - Unsteadiness and falls
 - Abnormal pull test - falls backwards .
 - Freezing phenomenon .

Rigidity or hypertonia

00:28:27

- Involuntary increase in the muscle tone
- Cog wheel or lead pipe
- By slow passive movements across the joints
- Rigidity is associated with pain and stiffness of muscle .
- Froment's Sign : Activity induced increase in contralateral rigidity

Hypertonia:



Gait dysfunction:

- Short shuffling gait, Festinant gait.
- Festination: Tendency to increase the velocity but with shorter steps.
- Narrow based gait in Parkinson's disease, Broad based in parkinson disease like in MSA-C, PSP
- Stooped posture with flexion of neck, trunk, knees.

Head to foot Features:

- Rest tremor
- Rigidity - lead pipe / cog wheel.
- Posture instability
- Bradykinesia
- Glabellar tap sign
- Reduced blinking
- Speech - Hypophonia
- Festinant gait
- micrographia
- Autonomic disturbances.



Sequence of Symptoms:

Tremor → Bradykinesia → Axial skeleton → Cognitive symptoms.

↓

Gait & Postural abnormalities

Sensory	Autonomic Dysfunction	Neuropsychiatric	Sleep Disorder
Pain	Orthostatic hypotension	Anxiety	Excessive daytime sleepiness
Hyposmia (loss of smell)	Erectile dysfunction	Apathy	Reduced sleep efficiency
	Constipation	Bradyphrenia (slowed thinking)	Reduced slow wave sleep
	Urinary urgency	Depression	REM sleep behavioral disorder (RBD)
		Dementia	Restless legs syndrome
		Hallucinations	

Differences between parkinson's disease and diffuse Lewy body dementia

00:38:10

Lewy bodies - are also seen in diffuse Lewy body dementia.

Comparison of Clinical Presentations of Parkinson's Disease Dementia and Dementia With Lewy Bodies

Parkinson's Disease Dementia	Dementia With Lewy bodies
Cognitive impairment occurs at least 12 months after motor manifestations of the disease (usually 4 to 5 years at least).	Cognitive impairment usually occurs within 12 months of motor manifestations of disease.
Hallucinations occur later and after Parkinson's disease medication use.	Hallucinations occur earlier and sometimes prior to Parkinson's disease medication use.
Tremor is common.	
Predominantly unilateral motor symptoms are common.	Bilateral motor symptoms are more common.
Axial symptoms and gait difficulty are less common.	Axial symptoms and gait difficulty are more common.

Active space

Atypical Parkinson's (or) Parkinson plus syndromes

00:43:00

1. Progressive Supranuclear Palsy (or) Steel Richardson Syndrome
2. Diffuse Lewy body Dementia
3. Multisystem Atrophy
4. Cortico Basal Degeneration .

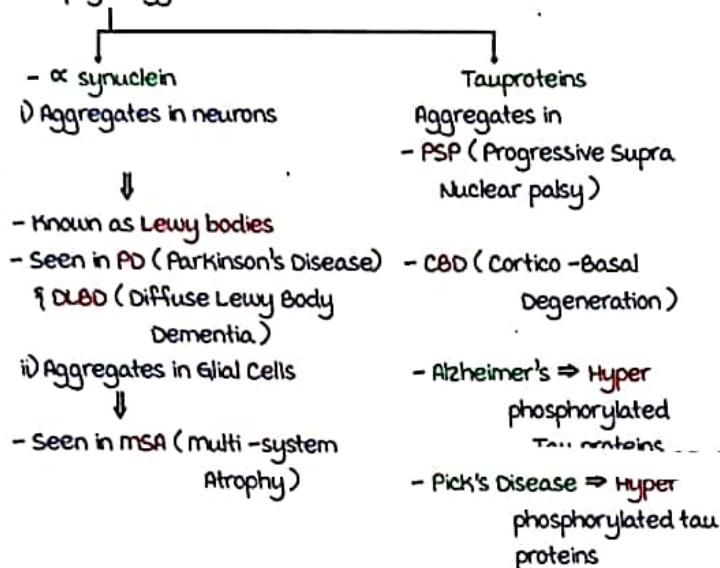
- Parkinson plus syndromes are suspected when :

- There is no response to L-dopa
- Absence of Rest tremor at presentation .
- Severe early onset ANS Symptoms
- Early dementia / hallucinations
- Cortical abnormalities → Apraxia
- Supranuclear Gaze Palsies .
- Predominant cerebellar or pyramidal finding
- Early onset repeated falls .
- Symmetrical bradykinesia

Active space

PARKINSON PLUS SYNDROME

Pathophysiology

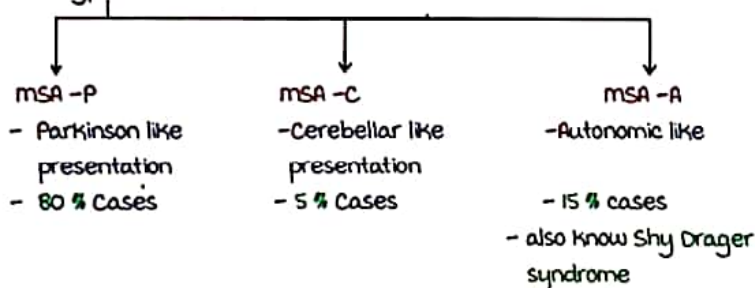


Multi - System Atrophy (MSA)

00:03:07

i) Parkinson Plus Syndrome

ii) Types



iii) Characteristic features

- Tremors at presentation - Absent (But may present later)
 - Cerebellar / Autonomic dysfunction (Shy Drager syndrome) - Present
 - Pyramidal involvement - present
 - Cervical dystonia - present
- iv) Glial cytoplasmic inclusion which stains for α-synuclein
- v) 90 % ⇒ unresponsive to L - dopa

- vi) Falls → less frequent
- vii) Jerky postural / rest tremor / loss of postural stability ⇒ occurs late
- viii) Cranio - cervical dystonia - present
- ix) High pitched dysarthria - present
- x) Radiological findings in MSA



Cruciform hyperintensity
(Hot cross bun sign)



Putamen rim
hyperintensity



Hot cross bun
sign



T₂W - MRI

- Putamen rim hyperintensity
- Cruciform Hyperintensity ⇒ Hot cross bun sign

Progressive Supranuclear Palsy [PSP]

00:11:10

- i) also known as Steele - Richardson Olszewski syndrome
- ii) Characteristic features
 - Extension hypertonia [On contrary, Parkinson - flexion Hypertonia]
 - Frequent falls
 - Eyelid apraxia ⇒ Down gaze palsy
 - Broad based gait
 - Retrocollis
 - Facial dystonia ⇒ Procerus / Surprise sign

- iii) A type of Tau proteinopathy
- iv) Tremors - uncommon
- v) Pseudo bulbar involvement [Bilateral corticobulbar +/- Corticospinal involvement]
 - spastic dysarthria
 - Emotional incontinence
- vi) Applause sign - present
- vii) Humming Bird sign on m R I [Atrophy of mid brain]

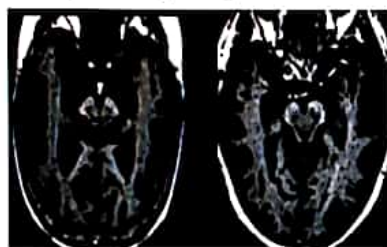


retrocollis



Facial dystonia

- viii) Frontal Release sign
- ix) Humming Bird sign / Penguin sign



labels of image above

- mid Brain - Atrophy of tegmentum
 - Cerebellum
 - Pons
- } - Normal



Corticobasal Ganglionic Degeneration (CBD)

00:18:48

D A type of Tauopathy

ii) Histo pathological difference between PSP & CBD

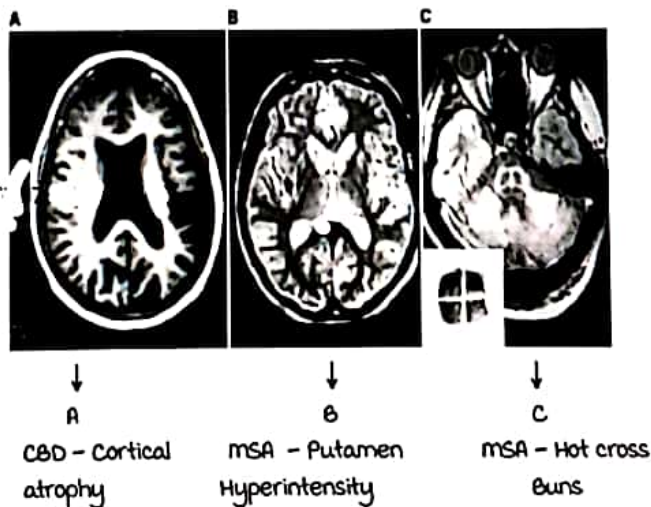


- a) PSP - tufted astrocyte
- b) CBD - astrocytic plaques

iii) CBD - Parkinson's motor onset with predominant Cortical Findings
+
MRI - Cortical atrophy

iv) Features in CBD

- a) Apraxia, Agnosia
- b) Alien limb phenomenon
- c) Asymmetrical dystonic contractions
- d) Dementia

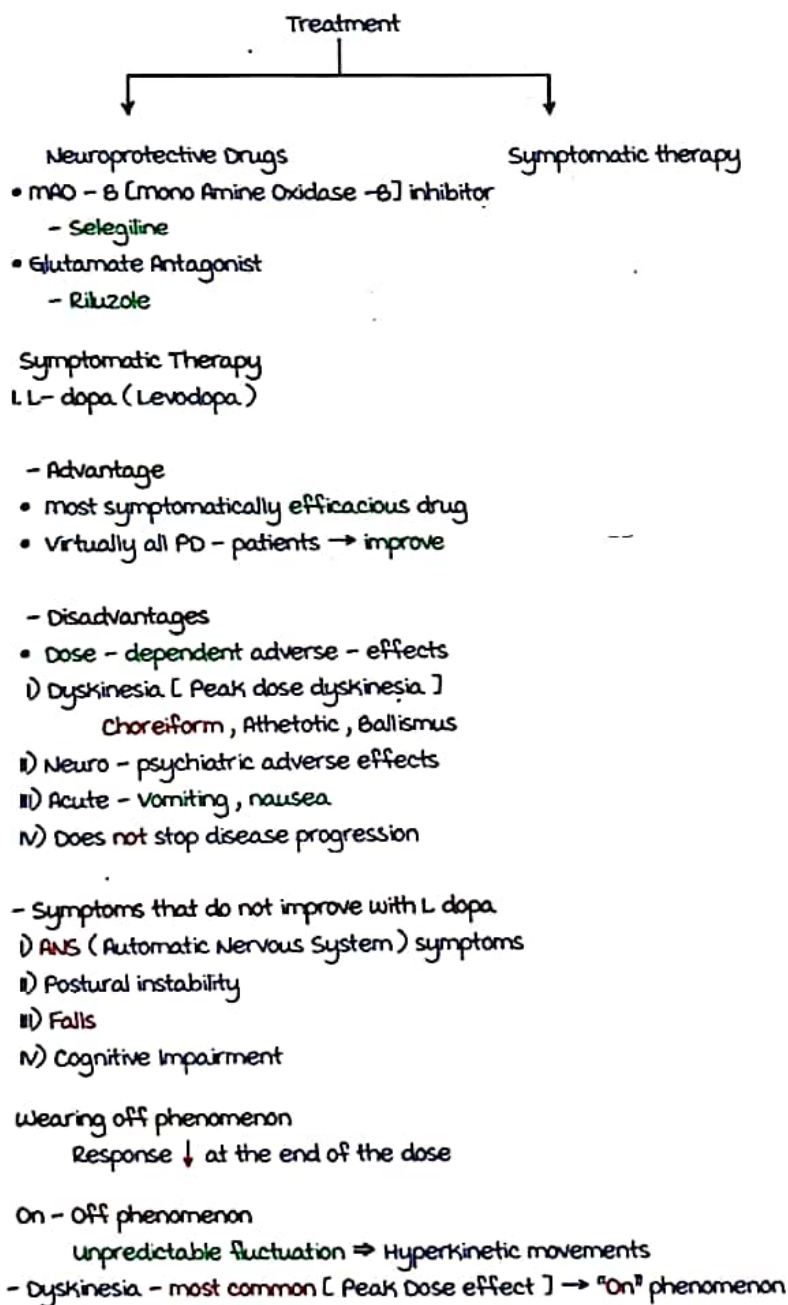


Active space

TREATMENT OF PARKINSON'S DISEASE & HYPERKINETIC DISORDERS

Treatment of Parkinson's disease (PD)

00:00:39



- Dystonia [Patients not responding to L-dopa] → "Off" phenomenon
- Diphasic dyskinesia [Dyskinesia - immobility - Dyskinesia]

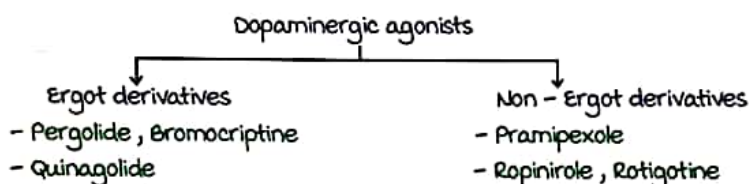
Pisa syndrome



[off period]

2. Dopaminergic Agonists

- L - dopa sparing effect
- ↓ motor complications



Advantages

- Efficacious when used as monotherapy / adjunct to L - dopa

Disadvantages

- Neuropsychiatric features
 - Hallucination, psychosis
- Efficacy - less [Compared to L - dopa]
- Does not completely prevent development of levodopa related motor complications
- Does not treat all features of PD
- Does not stop disease progression

3. COMT inhibitors

- Catechol - O - methyl Transferase Inhibitors
- Inhibits metabolism of dopamine
- Drugs : I) Tolcapone → inhibits both central & peripheral COMT
 II) Entacapone → inhibits only peripheral COMT
- ↓ Levodopa dose requirement by 25 %
- ↑ in on time

4. Centrally acting anticholinergics

- Drug : trihexyphenidyl
- Used in drug induced parkinsonism [parkinsonism tremor]
- No effect on rigidity / postural instability
- Has cognitive side effects

Other drugs used in parkinson's disease

00:12:17

5. Amantadine

- Advantages
 - mild anti parkinsonism action
 - Antidyskinetic effects [Rescue agent]

Disadvantages

- may develop tolerance
- Cognitive side effects

Treatment of early parkinson's disease

00:13:17

Patient < 60 yrs

- mild symptoms → Amantadine

Patient > 60 yrs or < 60 years with functional disability

- Start with dopaminergic agonist (DA)
- Add L - dopa when response is inadequate

Advantages of starting dopamine agonist (DA)

- DA are associated with ↓ risk for inducing MRF (motor related fluctuation) compared to L-dopa.
- Comparable anti - parkinsonian effect for initial 2-3 yrs
- Levodopa added to enhance clinical benefit (when response is inadequate)

Abnormal movements & related disorder

00:17:08

I. Chorea

Conditions in which chorea is evident :

- I) Acute rheumatic fever → Sydenham's chorea
- II) Huntington's chorea
- III) Chorea gravidarum

Dystonia, athetosis, hemiballismus

00:25:38

3. Dystonia

Types of neck dystonia



Torticollis



Laterocollis



Retrocollis



Antecollis

- A type of hyperkinesia
- Spontaneous, involuntary & sustained muscle contraction that forces the affected part of the body into abnormal movements / posture
- Types of dystonia : Cervical
 - Oromandibular
 - Spasmodic
 - Blepharospasm

4. Athetosis

- unilateral, slow, involuntary, rhythmic writhing movements
- more sustained & larger amplitude than chorea
- cause : Lesion in putamen

Pseudoathetosis

- Sensory ataxia
- Posterior column involvement

5. Hemiballismus

- wild, writhing movements
- Cause - lesion in the contralateral subthalamic nucleus

Note :**Brain pacemaker**

- Hemiballismus
- Transcranial deep brain stimulation

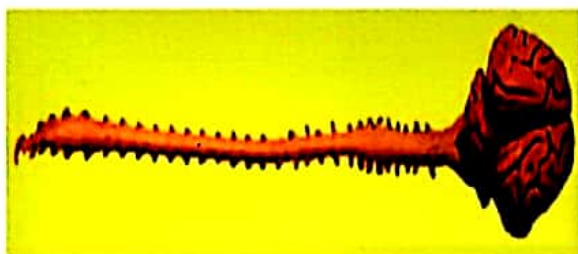


- Stimulation of subthalamic (or) Globus pallidus interna
- Very good impact on PD

SPINAL CORD - ANATOMY

Spinal Cord - Introduction

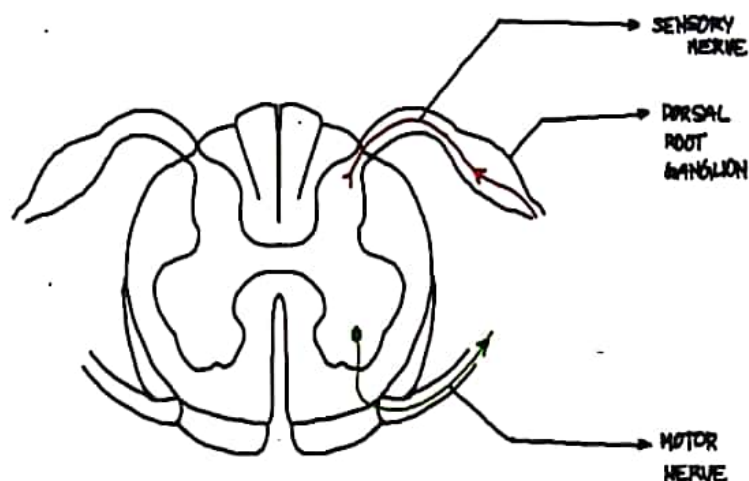
00:00:37



- Elongated cylindrical structure
- Extends from upper border of Atlas to lower border of L_1 (or)
 - Junction between L_1 & L_2 - adults
 - Junction between L_3 & L_4 - Children
- Continues above with medulla oblongata
- Foramen magnum to lower border of L_1
- 31 Segment & 33 vertebrae
- Vertebral canal - 70 cm long
- Spinal cord - 45 cm long
- Conus medullaris - S_3 , S_4 , S_5 Coccygeal
- Filum terminale - Extends from tip of conus medullaris to dorsum of 1st coccygeal vertebrae
- Vertebrae - Cervical - 7
 Thoracic - 12
 Lumbar - 5 $\Rightarrow$ 33 vertebrae
 Sacral - 5
 Coccygeal - 4
- Spinal nerves / spinal segments - Cervical - 8
 Thoracic - 12
 Lumbar - 5 $\Rightarrow$ 31 pairs of spinal nerve
 Sacral - 5
 Coccygeal - 1

Spinal Cord - Cross Sectional Anatomy

1. White matter of spinal cord
 - Fibres are called funiculus / tracts
 - Dorsal, ventral, lateral funiculi
2. Grey matter of spinal cord
 - motor neurons
3. Spinal nerve root



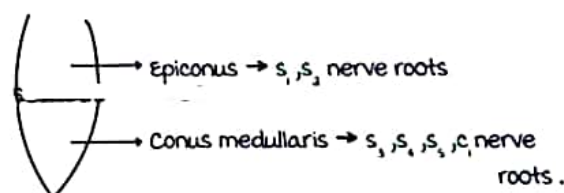
- Sensory nerve enters spinal cord
- Motor nerve leaves the spinal cord
- Spinal nerve root is formed by sensory nerve & motor nerve

Relation of spinal nerve roots to vertebrae

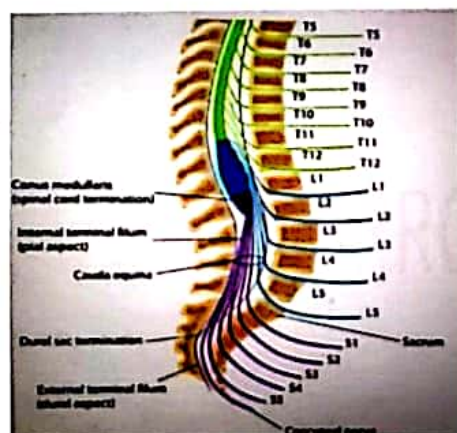
00:06:38

- Spinal cord ends at lower border of L_1
- Spinal nerve roots do not emerge in correspondence to vertebrae
- T_{12} vertebrae $\rightarrow L_1$ Spinal nerve root emerges
- T_{11} vertebrae $\rightarrow L_1$ & L_2 nerve root
- T_{10} vertebrae $\rightarrow L_1$ & L_2 nerve root

L_1 vertebra



Active space

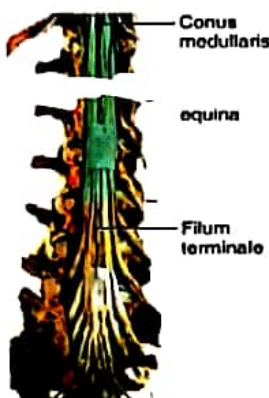


Spinal Cord Level	Corresponding Vertebral Body
Upper cervical	Same as cord level
Lower cervical	1 level higher
Upper thoracic	2 levels higher
Lower thoracic	2 to 3 levels higher
Lumbar	T10-T12
Sacral	T12-L1

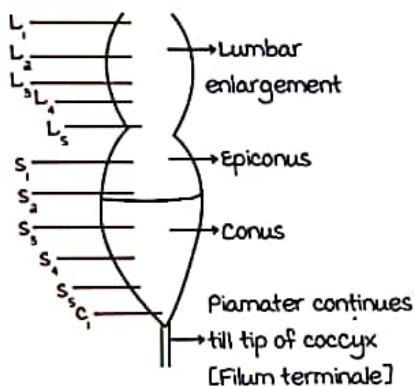
Conus medullaris, cauda equina, filum terminale

00:13:45

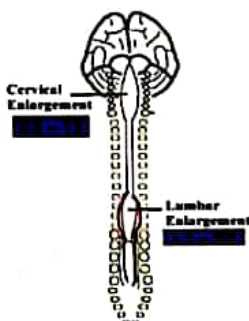
- **Conus medullaris**
Conical structure, continuous with filum terminale
- **Cauda Equina**
 - Sheath of nerve root from lumbar & caudal segments in subarachnoid space enlargement
 - Horse tail appearance
- **Filum terminale**
 - 20 cm long
 - Below the level of conus medullaris only pia mater is continued as a fibrous cord, extending to dorsum of C₁ (coccygeal) segment.



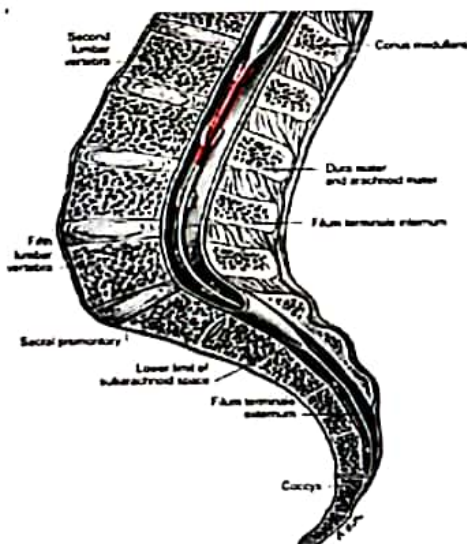
- **Cauda Equina** [L₁ - C₁ nerve roots]



Spinal enlargements



- **Cervical enlargement** [C₃ - T₂ Vertebrae]
- **Lumbar enlargement** [L₁ - S₃ Vertebrae]



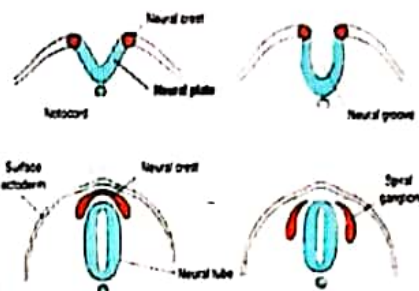
Active space

Spinal cord - general internal organisation

00:21:14

a. Spinal Cord - Embryology

- Spinal cord arises from
 - Caudal part of neural tube in the 4th week of embryonic life
- Spinal cord wall forms
 - 3 layers: Ependymal, mantle, marginal



b. Grey matter & white matter of spinal cord

i) Grey matter of spinal cord

- Fibres → Columns / tracts
- Has AHC (anterior horn cell)
 - ↓
 - medial group → Supplies axial muscles
 - lateral group → Supplies limb muscles
- Lesions
 - lesions up to AHC → UMN (upper motor neuron)
 - lesions from AHC → LMN (lower motor neuron)

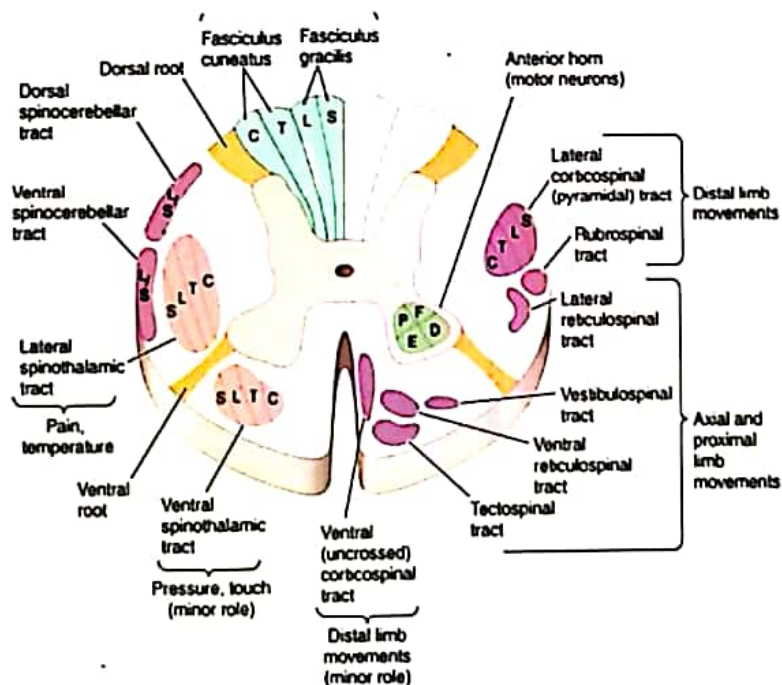
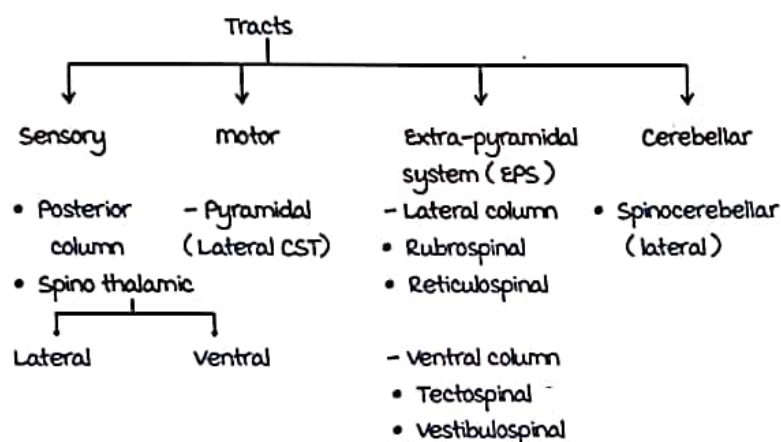
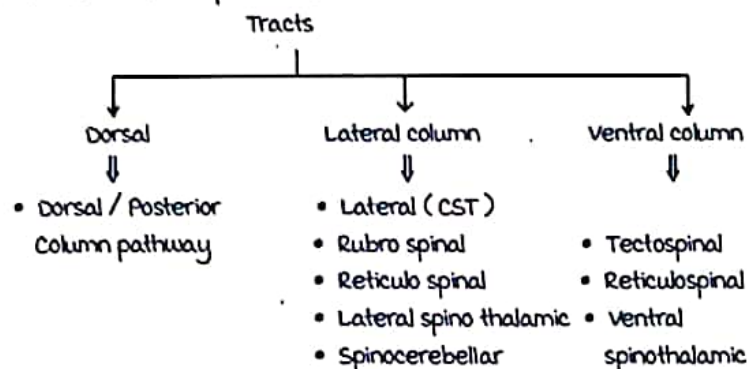


- Extra-Pyramidal → AHC ← Pyramidal
 [Cortico spinal tract (CST)]
 - Tecto spinal
 - Rubrospinal
 - Reticulospinal
 - Vestibulo Spinal tract
- (CBT) Cortico Bulbar Tract → Bulbar nuclei in brain stem

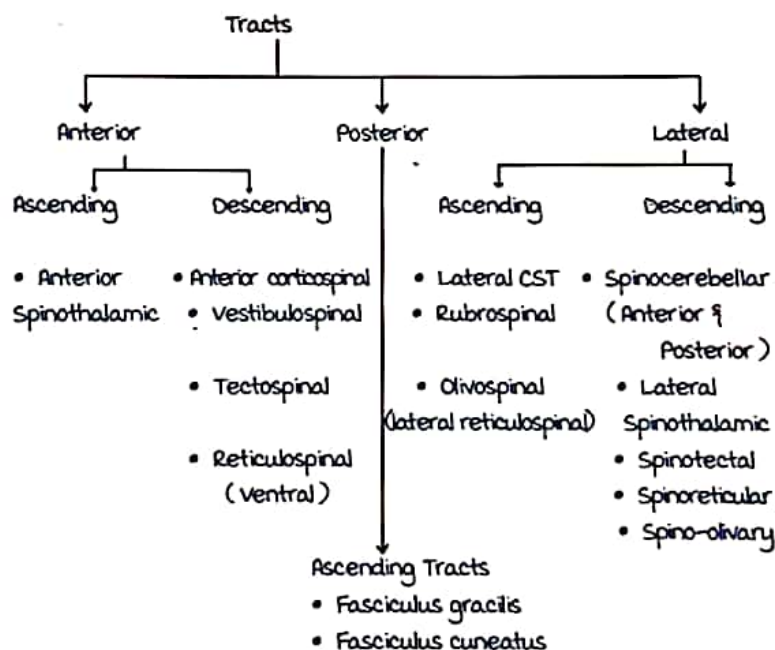
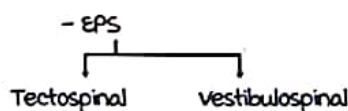
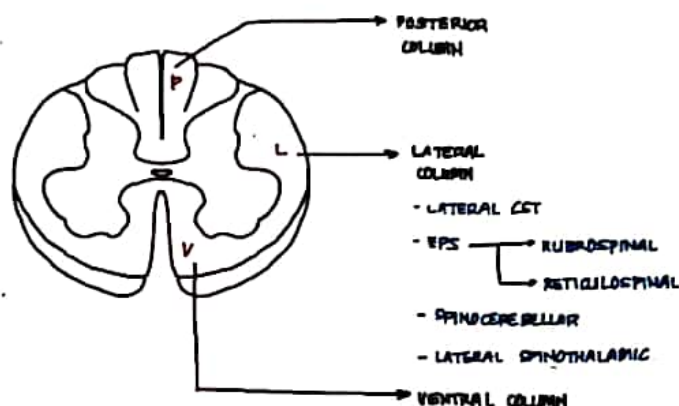
Lesion of the above tracts ⇒ UMN lesion

- Lesion at & Below AHC ⇒ LMN lesion
- Grey matter
 - Central column
 - H-Shaped lateral mass connected by grey commissure
 - Anterior, posterior & lateral columns

10) white matter of spinal cord



Active space



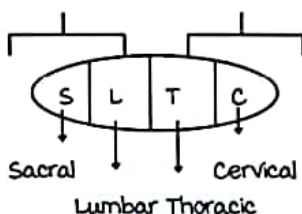
Active space

Ascending tracts in posterior column pathway

00:33:28

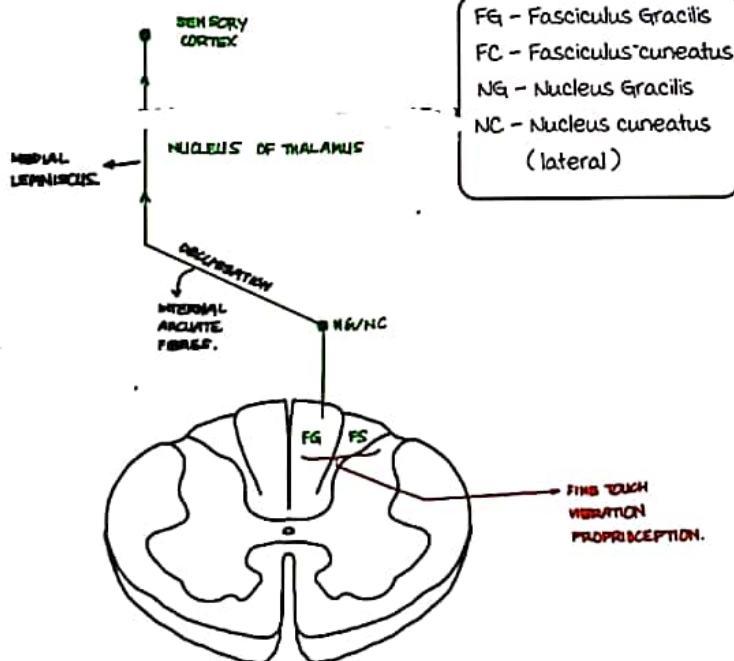
- Dorsal / Posterior column / medial lemniscal pathway
- Sensory
- Responsible for -
 - Fine touch
 - Vibration
 - Proprioception
- Tracts -

Fasciculus Gracilis (medial) Fasciculus Cuneatus (lateral)



Sensory cortex

Posterior Column:



Hemicordecotomy $\Rightarrow$ Loss of posterior column sensations of the same side

Spino Thalamic Tract

00:41:33

• Spinothalamic Tract

Ventral

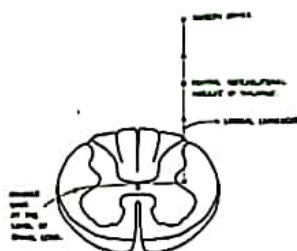
- Crude touch
- Pressure

Lateral

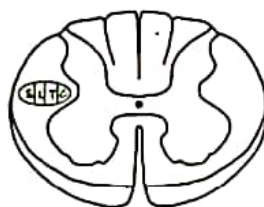
- Pain
- Temperature

- Spinothalamic Tract goes Lateral > Ventral
- Lateral spinothalamic Tract

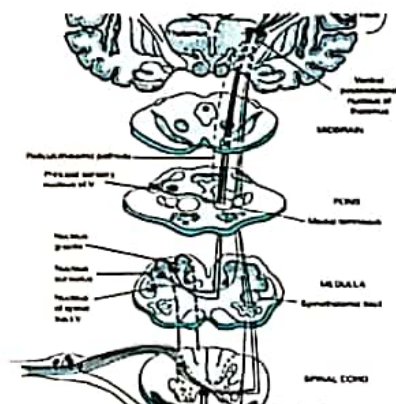
Crosses over
at the
level of spinal cord



Representation of fibres



- Cervical → Sacral
(medial) (Lateral)



Active space

Cortico Spinal Tract

00:44:50

Motor Pathway

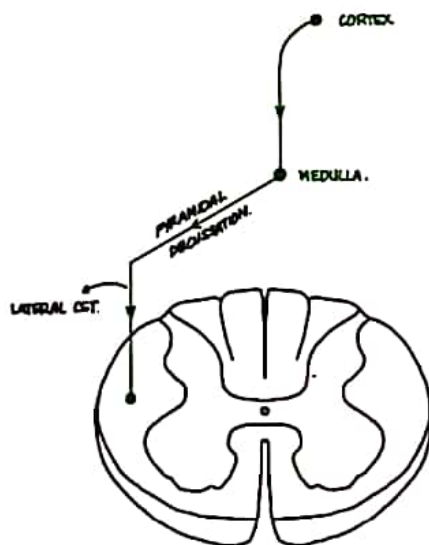
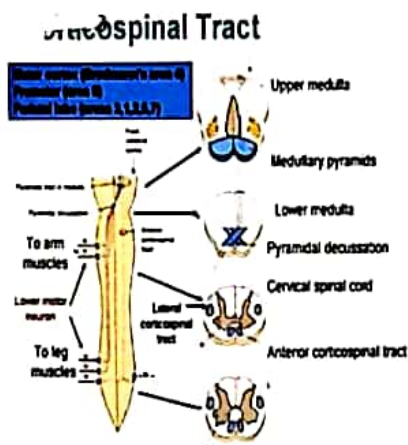
Pyramidal ↓ extra pyramidal system (EPS)

Lateral corticospinal

- Initiation & Partly integration of fine, skilled, distal voluntary movements

↓

Lesions → produces weakness



Hemicordectomy ⇒ Loss of lateral CST sensation of same side
Loss of lateral spinothalamic tract sensation of opposite side

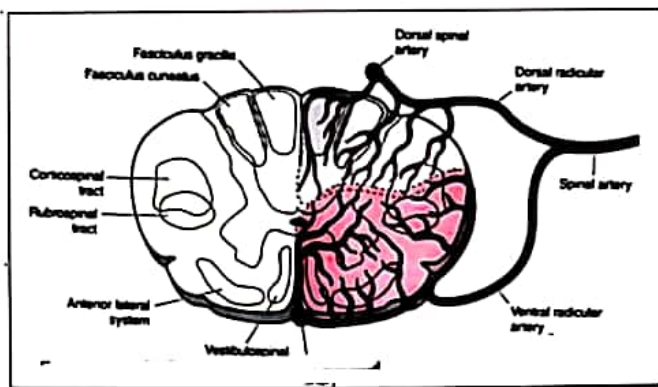
EPS - Tracts

- Vestibulospinal → Posture
- Tectospinal → Head & neck movements [vision, Auditory sense]
- Reticulospinal → Proximal upper limb movements.
- Rubrospinal → Rudimentary in humans

Active space

Spinal Cord - Blood Supply

00:50:26



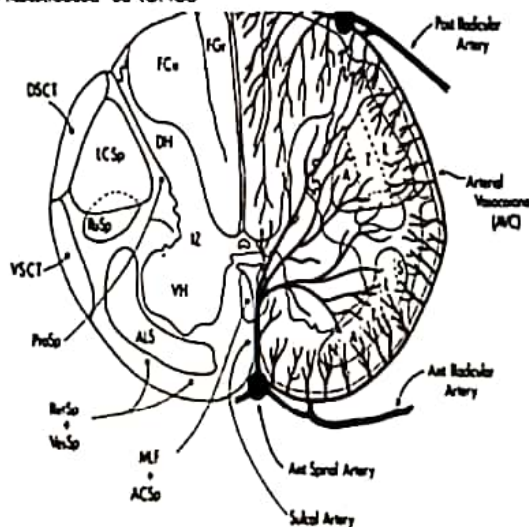
1. Anterior spinal artery

- Supplies ventral 2/3rd spinal cord [Anterior & Lateral column]
- 1 in number

2. Posterior spinal artery

- Supplies dorsal 1/3rd of spinal cord [Posterior Column]
- 2 in number

3. Radicular arteries

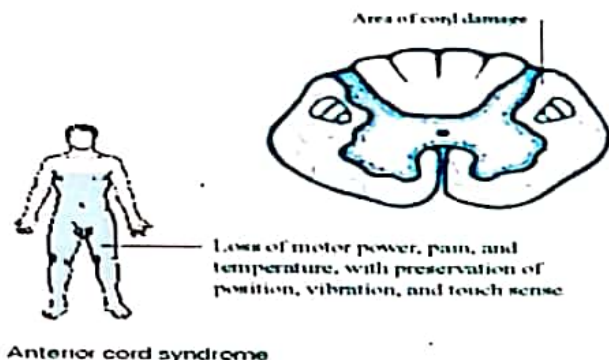


- i) upper half of cervical cord → No radicular arteries
- ii) Lower cervical & first 2 thoracic → 4 radicular arteries
- iii) mid thoracic → 1 radicular artery
- iv) Arterial radicularis magna → major blood supply to the lower 2/3rd (Lower thoracic to Coccygeal)
→ Known as artery of Adamkiewicz

Syndromes of spinal cord

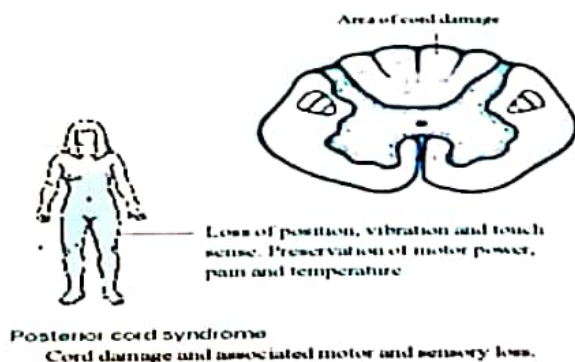
00:53:35

1. Anterior spinal artery syndrome



- Also known as anterior cord syndrome
- most common Cause - Trauma
- Loss → anterior 2/3rd of spinal cord
- Preserved → posterior 1/3rd
- Preserved sensations → Fine touch, Proprioception, Vibration
- Loss of CST, Spinothalamic tract below the level of lesion
- Loss of autonomic nervous system

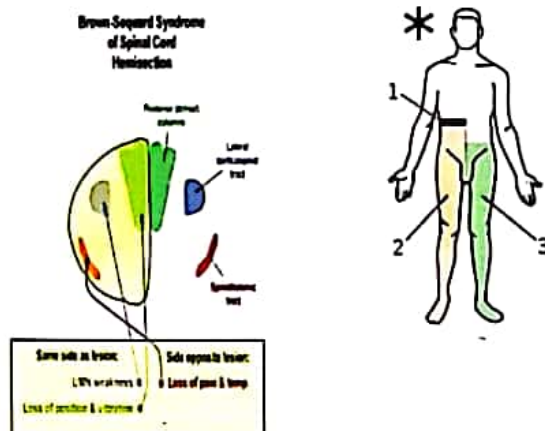
2. Posterior spinal artery syndrome



- most common cause - Trauma (Hyper - extension force)
- Loss → Posterior column fibres
- All the other fibres are preserved

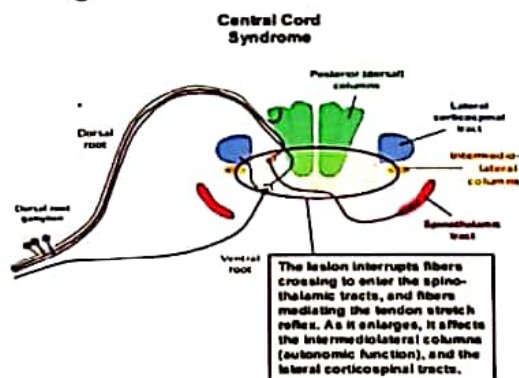
Active space

3. Brown - Sequard Syndrome



- Hemisection of the cord
- Same side as lesion
 - LMN weakness
 - Loss of position & vibration
- Opposite side of lesion
 - Loss of pain & temperature

4. Central cord syndrome



- Intramedullary lesion
- Dissociative sensory loss → involvement of spinothalamic with posterior column sparing
 of corticospinal tract → very late, sacral - sparing

MYELOPATHY APPROACH: COMPRESSIVE

- Paraplegia → lesion below the level of T_2
- Quadriplegia → lesion above the level of T_2

Level of lesion

00:00:54

- With respect to spinal nerve root
- Level → sensory, motor, spinal level, reflex
- Clinical manifestations based on level of lesion
 - Below the level of lesion
 - UMN (upper motor Neuron) weakness, exaggerated reflex (Hyperreflexia)
 - Complete sensory loss
 - Above the level of lesion

Complete sparing
 - At the level of lesion
 - Sensory component - Root pain / dysesthesia / paresthesia
 - motor component - LMN (Lower motor Neuron) weakness
 - Reflex component - lost
- Anatomical marking for spinal Nerves
 - T_4 → Nipple
 - T_5 → Xiphisternum
 - T_{10} → Umbilicus
- Foramen magnum → Around the clock weakness (or) Elsberg phenomenon [left upper limb → left lower limb → Right lower limb → Right upper limb weakness]
- Paraplegia → Below T_2
- Beevor's sign
 - To evaluate if paraplegia is below T_{10} or above T_{10}
 - Abdominal reflex
 - Preserved → lesion below T_{10}
 - Absent → lesion above T_{10}
 - on flexion of neck + contraction of abdominal muscles
 - if umbilicus moves 2-3cm upward → T_{10} pathology
 - [Reason - loss of tone lower abdominal muscles]
- i.e., upper abdominal reflex → preserved
 Lower abdominal reflex → lost } Beevor's - positive

Active space

- Superficial reflexes

- Abdominal reflex (T_{10}) [$T_1 - T_{12}$]
- Cremasteric (L_1)
- Plantar ($L_5 - S_1$)

i) All the above reflexes $\rightarrow$ lesion is above T_{10} (or) [$T_1 - T_{12}$]

ii) upper Abdominal reflex - present $\rightarrow$ lesion is below T_1

Lower Abdominal reflex - absent $\rightarrow$ lesion is around T_{10}

Cremasteric reflex - lost

Plantar - extensor

iii) Abdominal reflex (upper & Lower) - present

Cremasteric Reflex - Lost

lesion is
Between $T_{10} - L_1$

Spinal Nerve Root

$C_5, C_6 \rightarrow$ biceps, supinator

$C_7 \rightarrow$ triceps

$C_8, T_1 \rightarrow$ finger flexion

$L_1 \rightarrow$ hip flexion

$L_2, L_3, L_4 \rightarrow$ knee extension

$L_5, S_1 \rightarrow$ ankle dorsiflexion, hip extension

$S_2 \rightarrow$ plantar flexion

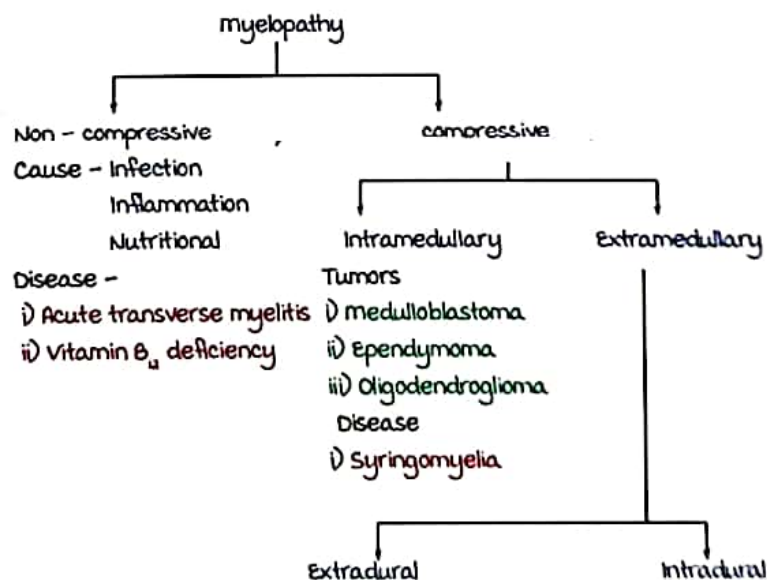
Reflexes

$L_4 \rightarrow$ knee jerk

$S_1 \rightarrow$ Ankle jerk

Myelopathies - classification

00:13:45

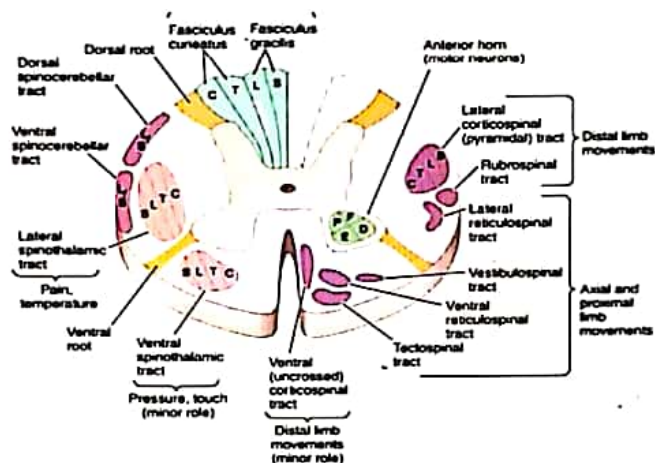


- i) Trauma
- ii) Tumor / metastasis
- iii) Aneurysm
- iv) TB/ syphilis /
Pyogenic infection
- i) Neurofibromatosis
- ii) meningioma
- iii) Arachnoid cyst
- iv) Pachymeningitis

Difference between extra medullary & intra - medullary 00:17:25

Extra - medullary lesions	Intra - medullary lesion
1. manifestations Stages 1 - Root Pain / Girdle pain - along the distribution of the root. - pain aggravates by Coughing. Stages 2 - Brown sequard syndrome Stages 3 - Complete cord transection Extramedullary 2. motor involvement → early 3. ANS - not very common 4. Not associated with LMN findings 5. Trophic Changes - may occur	Intramedullary 2. motor involvement → Late, sacral sparing 3. Dissociative sensory loss • Spinothalamic → lost • Posterior column → spared ie pain, temperature } lost Crude touch, pressure } 4. ANS [Autonomic Nervous system] - early onset - Predominantly Bowel & Bladder affected 5. AHC [Anterior Horn cell] - wasting, fasciculations, atrophy - LMN - due to cord involvement + - LMN - due to AHC involvement 6. Trophic changes - very common - due to loss of pain

CLINICAL FEATURE	INTRAMEDULLARY	EXTRAMEDULLARY
ROOT PAIN	—	+++++
DISSOCIATED SENSORY LOSS	+++++	—
SACRAL SPARING	+++++	—
TROPHIC CHANGES	+++++	—
PYRAMIDAL SIGNS	LATE	EARLY
LMN SIGNS	++	—
BOWEL/BLADDER	++	—
SPINAL DEFORMITY	—	+++
SPINAL TENDERNESS	—	+++
CSF PROTEINS	—	+++

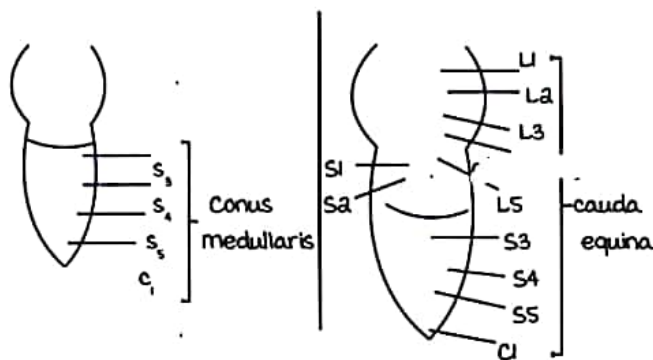


Conus Medullaris Vs Cauda Equina syndrome

00:27:15

Conus medullaris	Cauda equina
• Lesion $\rightarrow$ S₃, S₄, S₅, C₁ • Bilateral (B/L) • Acute onset • Bowel & bladder $\rightarrow$ Affected • Root pain $\ominus$ • Weakness $\ominus$ • Dissociative sensory loss $\oplus$ • Reflex - Bulbocavernosus - Anal } lost • B/L Saddle anaesthesia	• Lesion $\rightarrow$ L₁ $\rightarrow$ C₁ (root fibres) • Unilateral (U/L) • Gradual process • Asymmetrical • Bowel & bladder $\rightarrow$ Not affected • Root pain $\oplus$ • U/L motor weakness • Dissociative sensory loss $\ominus$ • Reflex - Any reflex can be lost • U/L - any pattern of anaesthesia can occur

Active space



Syringomyelia

00:33:00



- Cavitary expansion of central canal of spinal cord [especially - lower cervical]
- Congenital > Acquired
- Associated with Arnold - chiari type -1 [75% cases]
- Like intramedullary lesion [dissociative sensory loss]
- Involves spinothalamic tract [initially - U/L, Later -B/L]
- Syringomyelia → reaching medulla is syringobulbia
- seen in males > females
- Half - cape distribution of sensory loss
 [Loss of pain & sensory loss along chest , upper arm , shoulder]
- Onion peel pattern on face [loss of sensation of face]
- Compression of Ventral Horn cells → - Wasting of Thenar eminence
 - Forearm
 - Arm
- Spastic weakness
- Horner's syndrome
 [due to C8, T1 involvement]
- Kyphoscoliosis , Pes Cavus , Spina Bifida

Active space

MYELOPATHY APPROACH - NON - COMPRESSIVE

Acute transverse myelitis

00:00:12

- Inflammation of full thickness of spinal cord

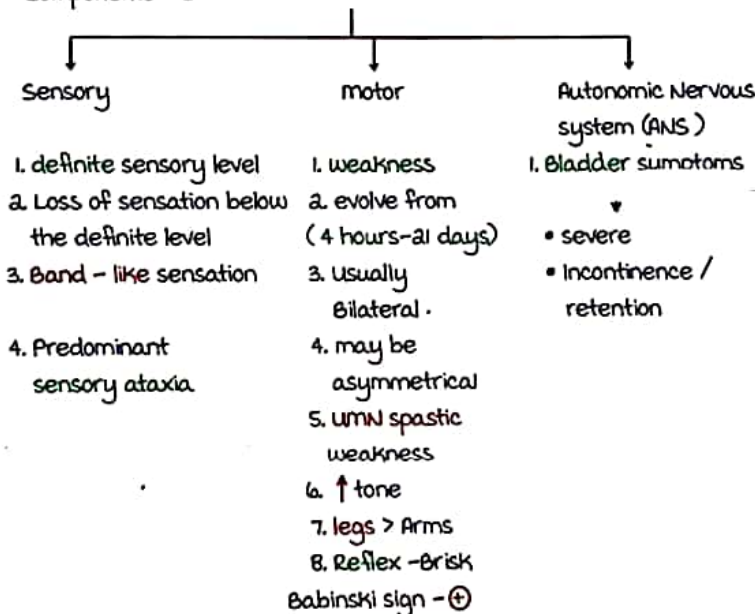
+

MRI changes & CSF changes

- Causes

- Post infectious (Post - viral)
- Post vaccination
- demyelination
 - Multiple sclerosis
 - Neuromyelitis optica

- Components - 3



Active space

Transverse myelitis Vs Guillain - Barre syndrome (GBS)

Acute Transverse myelitis	GBS
1. Lower limb > upper limb	1. progressive lower limb weakness [proximal > distal]
2. Symmetrical weakness	2. Ascends to upper limbs & bifacial weakness
3. Hyper-reflexia [Below the lesion]	3. Areflexia
4. Sensory ataxia	4. Normal sensory examination
5. Bladder symptoms ⊕	5. No Bladder symptoms
6. Band - like sensation ⊕	6. No Band - like sensation
7. definite sensory level	7. No level for sensory loss

MRI in Acute Transverse Myelitis



MRI - Gadolinium enhancement

Diagnostic criteria for Transverse myelitis

DIAGNOSTIC CRITERIA FOR TRANSVERSE MYELITIS

1. Bilateral (not necessarily symmetric) sensorimotor and autonomic spinal cord dysfunction
2. Clearly defined sensory level
3. Progression to nadir of clinical deficits between 4 hours and 21 days after symptom onset
4. Demonstration of spinal cord inflammation:
 1. cerebrospinal fluid pleocytosis or
 2. elevated IgG index, or
 3. MRI revealing a gadolinium-enhancing cord lesion
5. Exclusion of compressive, postradiation, neoplastic, and vascular causes

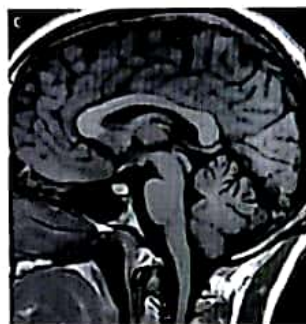
Treatment

1. Steroids → high dose
Good Response
2. Plasmapheresis
In patients unresponsive to steroids

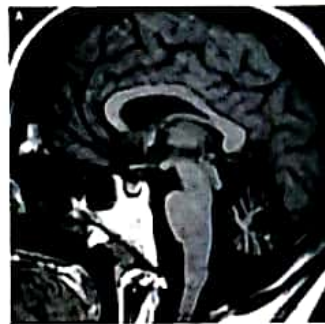
Friedreich Ataxia [FA]

00:08:33

- Autosomal recessive (more common)
 - early onset
- Autosomal dominant
 - late onset
- Males > Females
- Frataxin gene on chromosome 9
- Structures involved
 - i) DRG (Dorsal Root Ganglia) ⇒ Sensory ataxia, loss of reflex
 - ii) Spinal cord ⇒ - CST (Corticospinal Tract) ⇒ spino cerebellar involvement
 - Posterior column
 - iii) Peripheral nerve - demyelination
- Associated with myocardial fibrosis (90 % cases)
- Cerebellar findings
 - Dysarthric speech
 - Horizontal nystagmus
 - Sphincters unaffected
 - Lower limb reflexes with extensor - Absent
 - Plantar response - Present
 - Ataxic Gait
 - Romberg's sign - Positive
- Non - neurological findings
 - myocardial fibrosis
 - Optic atrophy
 - Pes cavus
 - Kyphoscoliosis
 - Hammer toe
 - Diabetes mellitus
 - Cardiomyopathy



Friedreich's Ataxia



Ataxia Telangiectasia

- Friedreich's Ataxia - Cerebellar anatomy - normal but;
 - Spinocerebellar tracts involved
- Ataxia Telangiectasia - Cerebellar atrophy seen

Sub Acute Combined Degeneration [SADC]

00:14:12

	FA	SADC
1. Tracts	DRG → Spinal cord → Peripheral nerves	Spinal cord [Posterior column → CST → Peripheral Nerve]
2. Reflex	Areflexia in lower limb	lost late due to peripheral neuropathy
3.	Sensory Ataxia	loss of vibration sense, tingling & numbness
4. Weakness	UMN weakness	UMN weakness
5. Associated	Cardiomyopathy / skeletal / optic atrophy	Vitamin B ₁₂ deficiency

Note

SADC

- UMN lesion cannot cause brisk reflex as they are already damaged by peripheral nerve lesion

Associated findings

- B/L optic neuropathy
- CNS changes : dementia
- Urinary retention

Tabes dorsalis

00:20:45

i) Structures involved -

DRG followed by spinal root

ii) Features :

DRG → Areflexia, Sensory ataxia

Spinal root → Severe root pain [due to posterior root lesion],

Loss of sensation, muscle

iii) Only LMN weakness

iv) Seen 15-20 yrs after syphilis infection

v) Bladder involvement

vi) Argyll Robertson pupil

vii) Posterior column - lost (due to DRG involvement)

viii) Extensor plantar - Absent

ACUTE BACTERIAL MENINGITIS

Definition: Acute purulent infection in the Sub Arachnoid Space

Bacterial meningitis - Only Acute

- Pt. presents within 24 hours of onset of symptoms
- 80% cases: CSF Culture positive and organism can be isolated.
- CSF acts as a culture medium for the organism to grow.

Organisms causing Acute bacterial meningitis:

- most common organism in Adults
 - Streptococcus Pneumoniae.
- Neisseria meningitidis.
- Group B streptococci
- Listeria monocytogenes
- H. influenza type B.

PATIENT GROUP	BACTERIAL PATHOGEN	RECOMMENDED EMPIRICAL THERAPY
AGE < 1 MONTH	ENTEROBACTERIACEAE, TREP AGALACTIAE AND LISTERIA	AMPICILLIN + 3 rd GEN CEPHALOSPORIN
1-23 MONTHS	S. AGALACTIAE, E. COLI, H. I, INFLUENZA, STREP. PNEUMONIA, N. MENINGITIDIS	AS ABOVE PLUS VANCOMYCIN IF PRSP SUSPECTED
2-50 YRS	STREP. PNEUMONIAE, N. M. ENINGITIDIS	3 rd GEN CEPHALOSPORIN PLUS VANCOMYCIN
> 50 YRS	S. PNEUMONIA, N. MENINGITIDIS, L. MONOCYTOGENES, group b strep	ABOVE PLUS AMPICILLIN
IMMUNO COMPROMISED	S. PNEUMONIA, L. MONOCYTOGENES, N. MENINGITIDIS, P. AERUGINOSA	CEFTAZIDIME + AMPI + VANCO
Post craniotomy, HEAD TRAUMA, CSF rhinorrhea	GNB	CEFTAZIDIME + VANCO
POST shunting or ommya reservoir	S. AUREUS, CONS	SAME AS ABOVE

- 2 - 50 years
 - Streptococcus pneumoniae - most common.
 - Neisseria meningitidis
 - Group B Streptococcus
 - H. influenza
 - Listeria monocytogenes
 - in immunocompromised (↓ in cell mediated immunity)
 - pregnancy

- > 50 years - *Listeria* is more common than *Hinfluenza*; but *Strep. pneumoniae* is most common.
- In Post shunting or Ommaya Reservoir (Intrathecal chemotherapy) - meningitis is caused by - *Staph aureus* > CNS.
- Post craniotomy meningitis
(or)
CSF rhinorrhea meningitis
(or)
Head injury associated meningitis
- In < 1 month - *E. coli* > *Strep. agalactiae*
- 1 month - 2 years - *Strep. agalactiae*.

Gram negative bacilli

Pathophysiology of acute bacterial meningitis

00:13:38

nasopharyngeal colonisation and intravascular extension of meningo cocci and pneumococci

not phagocytosed due to polysaccharide capsule

Reach choroid plexus epithelial cells

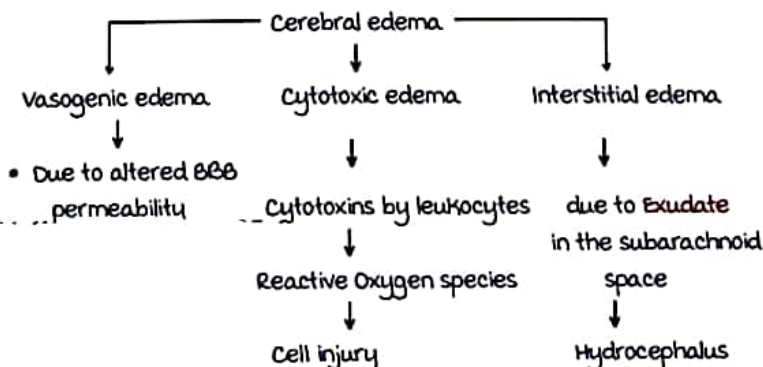
Gain access to CSF

Organism multiplies and release its Products

severe inflammatory response against bacterial products

- mediated by IL-1 β & TNF α
- It is combination of Interstitial, Cytotoxic and vasogenic edema.

- Cerebral edema $\rightarrow$ $\uparrow$ Intra Cranial Pressure and herniation.
- Alteration in Cerebral blood flow
- Ischaemia



Meningococcus

00:23:25

- Gram negative coccus
- Catalase +ve
- Oxidase +ve
- Diplococci - half moon shaped
 - it has capsular polysaccharide.
- Ferments Glucose and maltose - used to differentiate it from Gonococci.
- Strict aerobic organisms.
- Culture medium: modified Thayer martin medium.
- Group A - Epidemics
 - B - Epidemics and outbreaks
 - C - Outbreaks.
 - W-135 / Y - Sporadic cases.
- Most common - Group B. - In India
- No plasmid, no drug resistance.

In media - polyethanol sulfate - can augment the growth of the organism.

- It colonises with the help of Pili (fimbriae). Opacity associated protein.
- LPS - Lipooligosaccharide endotoxin → Endothelial injury.

↓
massive capillary leak
↓
Severe Hypotension.

- In blood - opsonised by C5b - C9
 - C5 - C9 deficiency → increased risk of meningococcal infection.
- uniformly susceptible to Penicillin.
- Drug of choice: Cephalosporins.
- If Penicillin allergy → Drug of choice: chloramphenicol.
- Carrier State: Cephalosporins, Rifampicin, ciprofloxacin - In 20%
- most common mode of spread - Nasopharynx - across the epithelial cells in membrane bound vacuole.
- Classical clinical finding: Purpuric rash.
 - Capillary leak → shock
 - Adrenal Hemorrhage - Waterhouse Friderichsen Syndrome.
- Increased risk of infection in C5 - C9 deficiency, hypogammaglobulinemia, hyposplenism.

Pneumococci

00:32:18

- Gram positive, α - hemolytic
- Catalase Negative, Fastidious.
- Flame or lanceolate shaped.
- Greenish coloured on Blood agar due to partial Hemolysis - draughtsman colony
- Bile soluble, Optochin susceptible, Inulin fermentors - used to differentiate it from strep. pneumonia and viridans.
- Antigens: Capsular polysaccharide, Pneumolysin, IgA1 protease.
- Abnormal protein which precipitates with somatic 'C' Antigen of Pneumococci - C - Reactive Protein.
- Rapid identification - Quellung's reaction.
- Adherence to Nasopharynx, Invasion is seen Only with Serotype 3.
- Pneumolysin - is a Cytolytic toxin which forms pores in the cell membrane.
- Risk factors:
 - >65 yrs. Age
 - Sickle cell Anaemia
 - Celiac disease
 - HIV
 - DM
 - Cochlear implant
 - CSF leak - G -ve organisms



Non infectious causes of meningitis:

1. Drug induced
2. Autoimmune: SLE
3. Chemical meningitis:
 - Due to tumor cells infiltrating into Subarachnoid Space
 - Seen with Craniopharyngioma, Dermoid cyst.
4. Post traumatic meningitis

Causes of aseptic meningitis:

- most common cause: Virus - Enterovirus Type 71
- HIV
- Listeria
- Drugs
- Partially treated meningitis.

Clinical features & diagnosis of meningitis

00:37:29

- classical triad: Fever + Neck stiffness + Altered Sensorium
[Lethargy, Drowsiness]
- most common symptom: Head ache

Nausea, vomiting +/-

Bed Side tests :

1. Kernigs Sign : Pain when the leg is extended from flexed position .
2. Brudzinski Sign : Passive flexion of neck

↓
Involuntary flexion of Hip and Knee .

- Done in Supine position .
- No lymphadenopathy
- Cerebral infarction at presentation - Pneumococci .
- Petechiae, Purpura , concurrent arthritis - N. meningitidis
- Seizure with Ataxia

Cranial nerve palsy

} Listeria

meningitis

↓
↑ Intracranial tension [ICT]

↓
Surest Sign : Papilledema - Fundus examination.

- If No papilledema
- No neurological deficit
- maintained consciousness
- No signs of increased ICT

↓
Definitive Diagnosis : Lumbar Puncture

↓
Start Antibiotics

If papilledema
Focal neurological deficits
Signs of raised ICT

↓
Antibiotics

Imaging needed before lumbar puncture :

- Focal Neurological Signs
- Immunocompromised adults
- Papilledema
- Recent onset seizures
- Impaired consciousness
- Hypertension and bradycardia .

Normal values of CSF in adults

00:48:10

- Colourless
- Specific gravity : 1.006 - 1.008
- Opening Pressure : 50 - 180 mm H₂O
- Proteins : 20 - 45 mg /dl .

- Sugar : 2 / 3rd of Blood Sugar = 40 - 70 mg/dl .
CSF
- S . glucose = 0.6
- Cellularity : < 5 WBCs
- PH : 7.28 - 7.32
- Chloride : 115 - 130 mcg/L
- LDH : 10 % of Serum levels .

Normal	Acute bacterial meningitis
• Pressure : 50-150 mm H ₂ O	↑ ↑ ↑ In severe cases : >400mm of H ₂ O
• Colour : colourless	• Cloudy
• Proteins : 20 - 45 mg/dl	• > 100 mg/dl
• Sugars : CSF = 0.6 S - glucose	< 0.4 - Severe bacterial meningitis .
• Cellularity : Normal (upto 5 W.B.C's)	• High . (>1000 - 50,000 cells) Predominant cells: Neutrophils

Investigation to detect the organism :

- Previously : Latex agglutination test
- Now : CSF - PCR
- CSF - lactate : ↑ ↑ in bacterial meningitis .
- CSF - Procalcitonin : ↑ ↑ in bacterial meningitis .
- Limulus lysate test : Gram -ve Organisms

Treatment of Acute bacterial meningitis

00:56:47

- Immunocompetent Adult (<50y) :
 - meningococci
 - Pneumococci
- Empirical therapy : Inj. Ceftriaxone 2gm IV BD
+
Vancomycin . 1gm IV BD
- Adult (>50y) :
 - Listeria is also common - Intrinsically resistant to Cephalosporin.
- Empirical therapy : Inj. Ceftriaxone 2gm IV BD + Vancomycin 1gm IV BD + Ampicillin (for listeria)

monitoring :

- Check for ↑ ICT and impending on herniation : check for pupillary reaction



- Hutchinson's pupil .
- monitor S . Na⁺ - for SIADH
- Severe listeriosis : Ampicillin + Gentamicin
DOC: Ceftriaxone + Vancomycin.

Bacterial Meningitis

Pneumococcal meningitis :

- Follows nasopharyngeal colonisation .
- Focus of infection elsewhere
- most Severe form of meningitis - can cause ischaemia .
- Complications : Aphasia and Cranial neuropathy
- High CSF Opening pressure
- Steroids in Pneumococcus :
 - Steroids are added in Bacterial meningitis
 - Steroid of choice : Dexamethasone . x 3 - 5 days - 0.5 mg / kg
Q6h
[15-20 mins before the Antibiotics]

meningococcal meningitis :

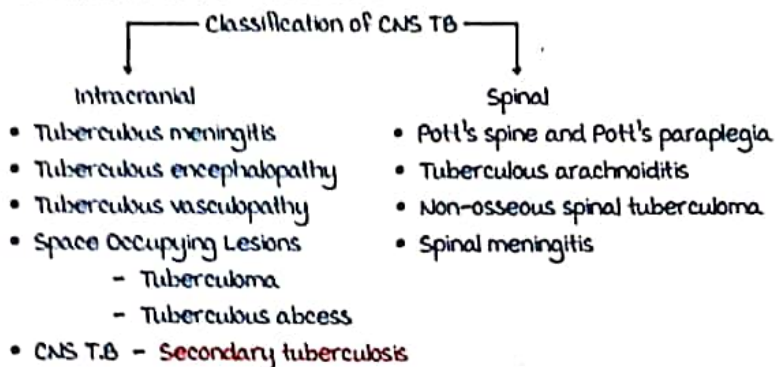
- Septicemia , DIC , shock , Adrenal Hemorrhage, Arthritis
- Rash - Non blanching
- Classical triad : less common
- Gram negative diplococci
- Better Prognosis .

Listeria monocytogenes :

- Gram positive bacillus
- Slow tumbling motility at 25° C
- Growth at 4° C
- Food poisoning : Soft cheese, Hot dogs, milk and Salads .
- Defect in CMI is mandatory .
- Organism cannot be cultured .
- Rhombencephalitis : Ataxia
myoclonic seizure
Cranial nerve palsy
- Intrinsically resistant to Cephalosporin .
- Ampicillin + Gentamycin - Treatment .
- Penicillin Allergy : Cotrimoxazole .
- Lymphocytic pleocytosis .

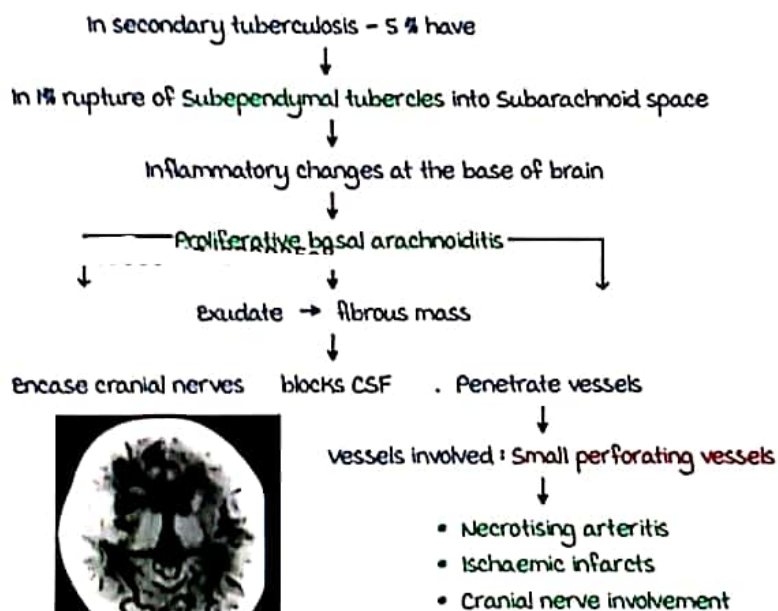
TUBERCULAR MENINGITIS

Classification of CNS - tuberculosis :



Pathogenesis of tubercular meningitis :

00:01:40



Plain CT Brain: infarcts in right BG and internal capsule

Diagnostic triad of tubercular meningitis

00:07:10

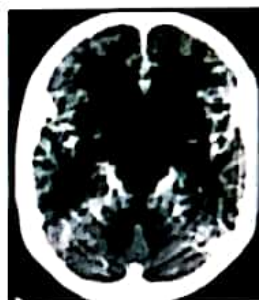
- 1) Presence of basal exudates
 - 2) Infarcts
 - 3) Hydrocephalus
- Specificity : **100%**
 - Lower Sensitivity

• Most common manifestation of CNS TB in all age groups.

• Meningeal enhancement has been found in up to 90% of cases and is considered to be the most sensitive feature of tubercular meningitis.



Axial T1C - florid meningeal enhancement, most pronounced within the basal cisterns



CT - acute hydrocephalus and meningeal enhancement.

• meningeal enhancement - On non-contrast imaging

• Differential diagnosis :

- mass lesion
- CNS tuberculoma
- Neurocysticercosis



T2-weighted MRI of a biopsy-proven, right parietal tuberculoma. Note the low-signal-intensity rim of the lesion and the surrounding hyperintense vasogenic edema.

Clinical features of T.B. Meningitis :

00:11:47

- Subacute presentation → 2-3 weeks
- It has 3 phases :

i Prodromal phase :

- Low grade fever for 2-3 weeks
- General malaise, head ache
- Altered behaviour pattern, ↑ ESR

ii meningitis phase :

- Severe headache and signs of meningeal irritation
- Vomiting

iii Paralytic phase



- Altered consciousness/Stupor/Coma.

Cerebrospinal fluid (CSF) findings in TB Meningitis 00:15:35

	Normal	Bacterial	TB
CSF pressure	50-150 mm H ₂ O	> 200 mm H ₂ O > 400 mm H ₂ O (in severe cases)	↑↑ > 200 mm H ₂ O
Protein	20-45 mg/dl	> 100 mg/dl	100-500 mg/dl
CSF/serum glucose (sugars)	0.6	< 0.4	0.4-0.6
Cellularity	upto 5 WBCs	↑↑	100-500 cells (lymphocytes mostly)

Early paradox:

In early phase → in CSF examination → PMNs predominate
(1-10 days) (Poly morpho Nuclear cells)

Therapeutic paradox:

After starting ATT → in CSF examination → Again PMNs are seen

- ADA levels → 10 U/litre → suggestive of TB
- Subacute onset of nerve root and cord compression signs
- Slowly progressive dementia - Suggestive of TB
- CSF lactate } Procalcitonin } favours Bacterial meningitis
- CSF chloride ↓↓ → favours TB meningitis
- In elderly → CSF is acellular sometimes (75 years)

Treatment: 2HRZE + 7-9 months HRE

Diagnosis: CSF Genexpert - by MTB/RIF

- Nucleic acid amplification method

Tuberculoma 00:21:50

- Presents as a ring enhancing lesion on imaging
- Differential diagnosis:
 - Tuberculoma
 - Neurocysticercosis

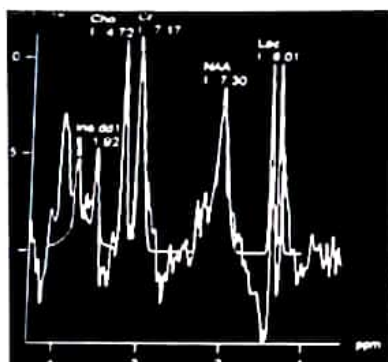
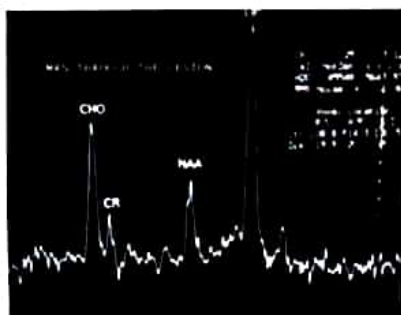
tuberculoma

- Larger (>20 mm)
- Irregular
- midline shift +/-
- variable intensity

neurocysticercosis

- Smaller
- Regular
- Not seen
- T₁ - Hypointense

MR Spectroscopy :
Lipid and choline peak



Lactate, N -acetylaspartate,
Creatinine, choline peaks

Eosinophilic meningitis

00:26:30

- >10 eosinophils/ μ l of CSF
- Major Parasites :
 - *Angiostrongylus cantonensis*
 - *Gnathostoma*
- Rarely :
 - *Schistosoma*
 - *Cysticercosis*
 - *Toxoplasma*

Treatment : aHRZE + 7-9 months HRE

Diagnosis : CSF Gene xpert - by m.TB /RIF

- Nucleic acid amplification method

Active space

VIRAL MENINGOENCEPHALITIS

Viral meningitis

- most common organism: Enterovirus (type 71)

HSV - 2

VZV

Viral encephalitis:

- most common organism: HSV - 1
- most common cause for epidemics of viral encephalitis (in Asians) → Arbovirus → Japanese encephalitis

Viral meningitis

- Benign
- Rare
- Clinical Features:

Non-specific prodrome with fever
(2-3 days)

↓
Remission

↓
Fever returns + meningeal symptoms

↓
Headache / nausea, vomiting / photophobia
Terminal neck stiffness / no altered sensorium

↓
Good recovery

Active space

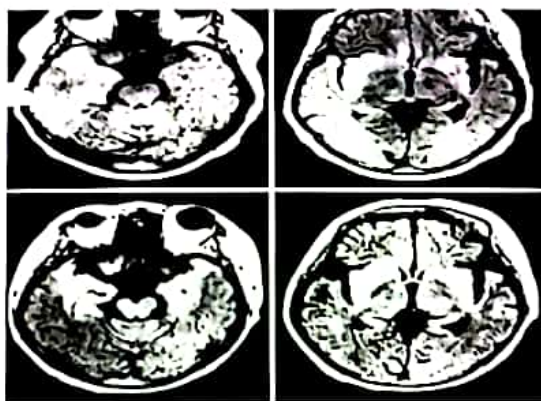
CSF findings

	Normal	Bacterial	TB	Viral
Pressure	5-150 mm H ₂ O	↑↑↑	↑↑↑	Normal to ↑ (<200 mm H ₂ O)
Cells	< 5 cells	↑↑	100 - 500	100-300 (< 300 cells)
Protein	20-45 mg /dl	↑, >100 mg/dl	↑↑, 100- 500 mg/dl	50-100 mg /dl
Sugars CSF / S. glu- cose	0/6	< 0/6 0.4-0/6 <0.4 (very severe)	0.4-0/6	Normal

Viral encephalitis

00:06:58

- Arboviruses and HSV -1
- Hemorrhagic necrosis of inferomedial temporal lobe and frontal lobe
- Clinically more severe than meningitis
 - Acute onset brain parenchymal disease
 - Seizures (status epilepticus)
- +
 - Fever + Personality changes
 - Behavioural changes
- CSF shows lymphocytic pleocytosis
- MRI : Bilateral temporal lobe hyper intensities (T₂)



JE show bilateral thalamic hyperintensities

- Diagnosis : antigen detection in CSF by PCR
anti JE , anti HSV
- EEG : PLED
(Periodic lateralized epileptiform discharges)

- Treatment : IV Acyclovir 10 mg/kg tds
- D/D : Autoimmune encephalitis (anti NMDA)
Paraneoplastic (anti Hu, anti Yo)

Cryptococcal (fungal) meningitis

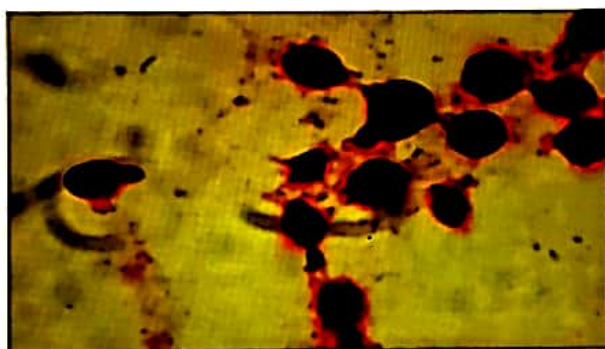
00:15:40

- Causative agent : *Cryptococcus neoformans*
through inhalation of spores
- Seen in immunocompromised (HIV)
- Subacute presentation - 1-3 weeks
- High predilection for CNS : can cross blood brain barrier

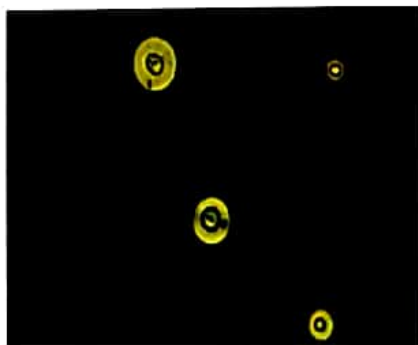
In CSF,

pressure	↑ ↑ ↑ 400-500 mm H ₂ O
cells	< 50/ml
protein	↑
sugar	↓ ; < 100mg/dl

- angioinvasion : invasion of blood vessels
- Investigations :
 - Gram staining of CSF : yeast like forms



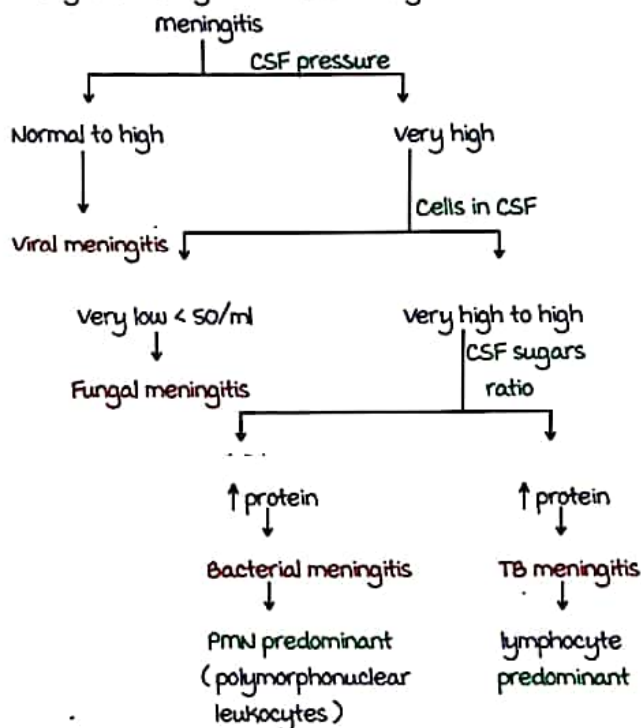
- Confirmed by India ink staining
clear zone around each yeast cell



- Cryptococcal antigen detection in CSF (fastest) by PCR or Latex agglutination

- Treatment : Liposomal Amphotericin B + 5- Fluorocytosine

Algorithm to diagnose meningitis from CSF findings



APPROACH TO UMN PATHOLOGY

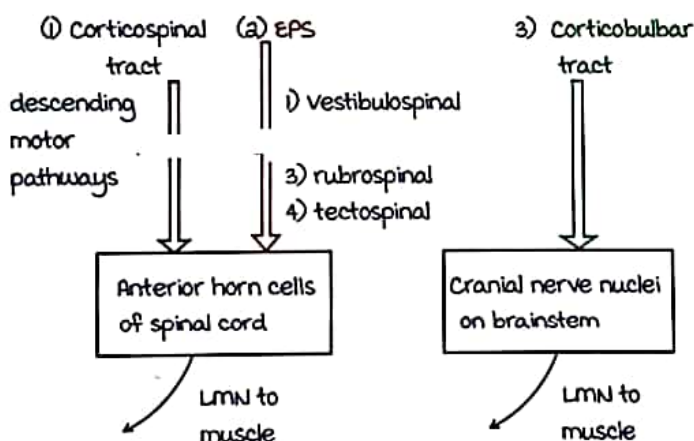
Introduction

00:00:55

- Hemiplegia :
 - Weakness : Corticospinal tract or Pyramidal tract involved (major motor pathology)
 - Spasticity : increased tone
 - hyperreflexia
- Pyramidal tract : initiation of fine, skilled, voluntary (distal) movements.
- EPS (Extra pyramidal system) : modulating and regulating movement planning, sequence and organisation (Basal ganglia.)
- Cerebellum : finesse to the movement

Upper motor neurons

00:06:08



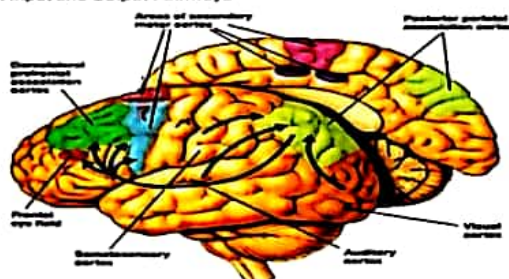
Upper motor neurons

- Pyramidal tract fibres
 - Extra pyramidal fibres
 - Corticobulbar fibres
- descending motor systems which merge on the anterior horn cells of spinal cord or cranial nerve nuclei on brainstem

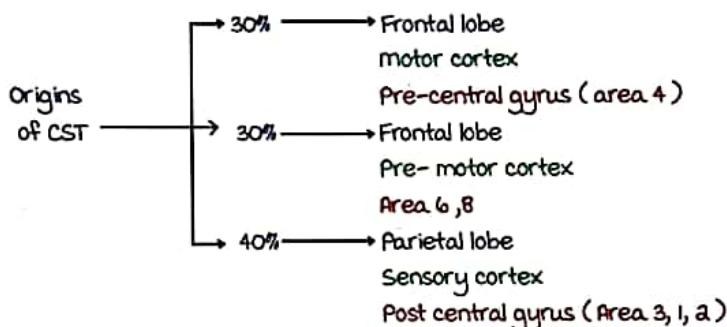
Origin of corticospinal tract

00:14:18

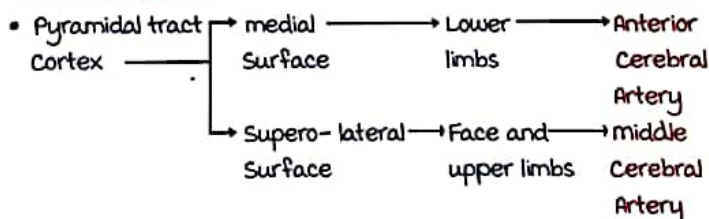
► Cortical Input and Output Pathways



• Origin of Corticospinal Tract (CST)



- Pyramidal cells or giant pyramidal cells of Betz are seen in layer 5 of motor cortex

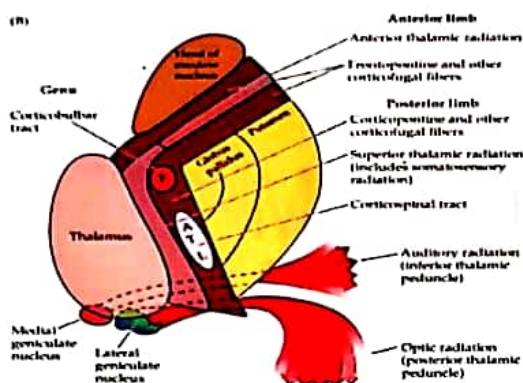


Anatomy of internal capsule

00:21:12

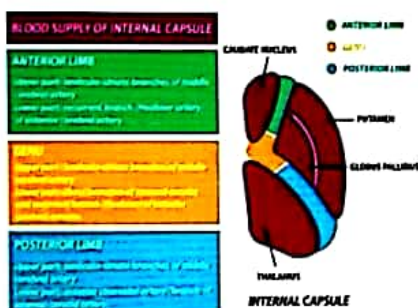
Internal capsule

- Anterior limb → Frontopontine fibres, anterior thalamic radiations
- Genu → Corticobulbar fibres
- Posterior limb → CST (anterior 2/3rd), superior thalamic radiations
- Optic radiation → Lateral geniculate body
- Auditory radiation → medial geniculate body



Blood supply of internal capsule

00:26:21



Anterior limb	Upper	Lenticulostriate branch of MCA
	Lower	recurrent branch of ACA (Heubner's artery)
Genu	Upper	Lenticulostriate branch of MCA
	Lower	directly supplied by ICA
Posterior limb	Upper	Lenticulostriate branch of MCA
	Lower	Anterior choroidal

Lesions of internal capsule

00:28:54

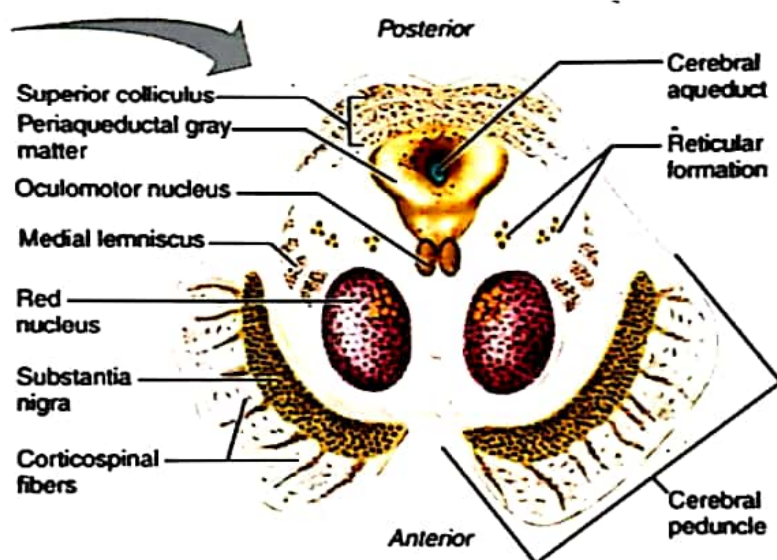
- Characterised by C/L:
 - Hemiplegia
 - Hemisensory loss
 - Homonymous hemianopia
 - Half (lower) of face affected

Active space

- Every cranial nerve → Bilateral representation nuclei
 - Exception: **Facial nerve nucleus**
 - Upper part → bilateral innervation
 - Lower part → unilateral innervation
 - In UMN lesions, lower half of face is affected while upper part of face is spared.
 - Angle of mouth deviated to opposite side

Lesions of brainstem

00:34:09



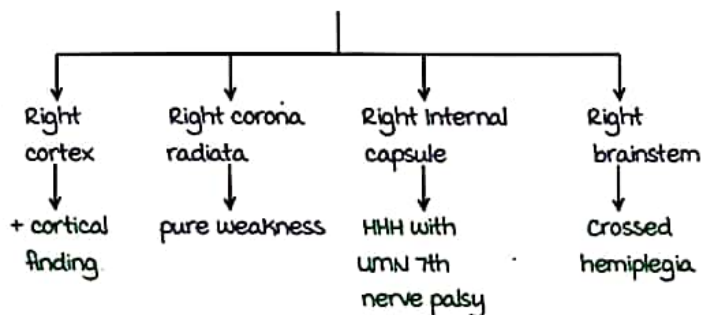
- middle 3/5th of cerebral peduncle → Corticospinal tracts (lateral)
Corticobulbar tracts (medial)
- They are characterised by ~~Crossed~~ **crossed** hemiplegia → Ipsilateral LMN cranial nerve palsy
+
Contralateral weakness
- Corticospinal tract is present as disjointed fascicles at basilar part of pons.
- Corticospinal tract decussates at the pyramidal level in the caudal medulla.
- 50% cervical
20% thoracic
30% lumbosacral portion

Clinical features of pyramidal lesions

00:42:40

Example: Acute onset weakness of Left upper and lower limb spasticity & hyperreflexia

Left-sided UMN hemiplegia involving either



- When CST is involved, look for pyramidal pattern of weakness. It is as follows:
 - Lower facial involvement
 - Voluntary > emotional
 - deglutition / articulation not affected
 - Voluntary skilled learned action most affected
 - Wrist / fingers / elbow extensors / supinators / abduction and external rotation of shoulders are affected.
 - Hip flexion and internal rotation of knee Flexion / dorsiflexion / eversion at ankle in also lost

Clinical manifestations of CST:

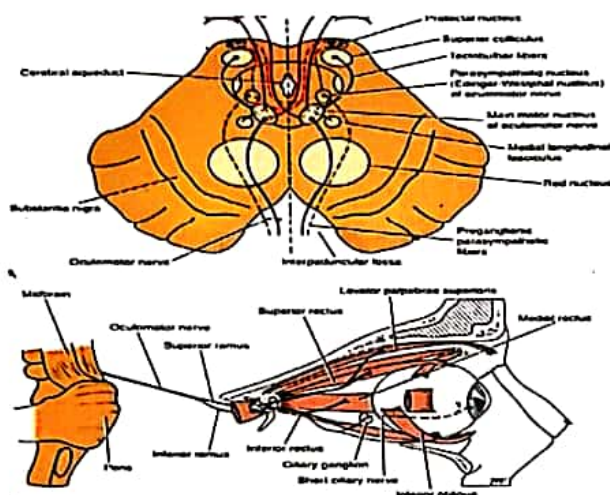
- Loss of skilled voluntary movement
- Impairment of integration of movement
- Over activity of lower segmental centres due to loss of inhibition
- Disrupted movement in contrast to specific muscles
- Others: Spasticity
 - Clasp-knife phenomenon
 - Reflexes ++
 - Power loss
 - Sensory (more at level of internal capsule)

CRANIAL NERVES - 1

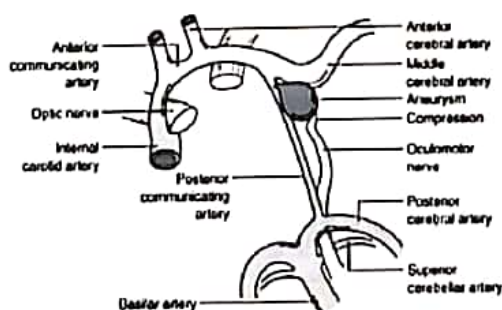
Cranial nerve III : Oculomotor

00:01:23

Origin : mid brain - Superior colliculus (ventral to cerebellar aqueduct).



- Parasympathetic → Via ciliary ganglion → Sphincter pupillae, Ciliaris (Pupil constriction)
- motor Nerve : Extraocular muscles (IO, SR, IR, MR, LPS) (no sensory)
- Single unpaired nucleus for LPS ;
- Edinger Westphal nucleus (EW) → Light reflex paired nucleus for MR, IR, IO, SR
- Superior Rectus → Contralateral supply by 3rd nerve nucleus.
- Rest of the muscle → Ipsilateral supply
- Nuclear lesion : bilateral ptosis + contralateral superior rectus palsy
- For convergence → Single unpaired nucleus.
- At level of Interpeduncular fossa : Subarachnoid course



Active space

- Passes between
 - Above : Posterior-cerebral Artery
 - Below : Superior cerebellar Artery

Post-Communicating Artery aneurysm

00:11:35

- Lateral to Post-Communicating Artery coursing anteriorly & pierce the dura
- In Aneurysm of Post-Communicating artery (PCOM) Compression of CN III

Nerve fibers in CN III

- Superficial : Peripheral parasympathetic fibers → Pial vessels
- Deep : motor fibers → vasa nervorum

- PCOM Aneurysm → Pupil involvement (or)

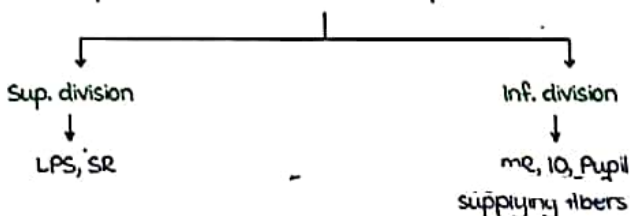
↑ ICT or Herniation through uncus

- DM → Involve vasa nervorum → pupil sparing IIIrd Nerve palsy

At the level of cavernous sinus : lateral wall →

III
IV
V₁
V₂

At the level of sup. orbital fissure : divides into 2 parts

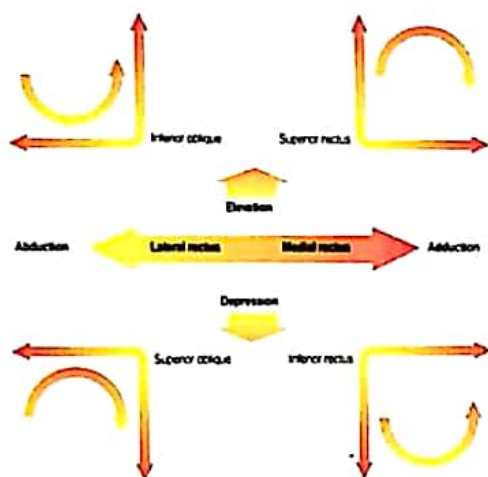
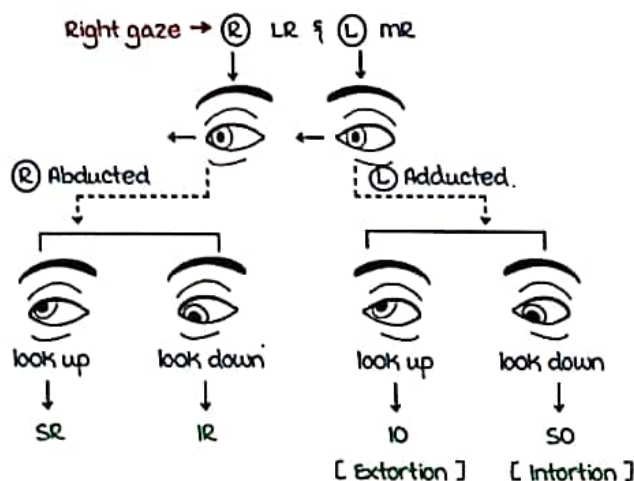


Ocular movements

00:16:30

Yoke muscle : SR ↔ IO, RR ↔ SO, MR ↔ LR

- Recti → origin : Annulus of Zinn
Insertion : Sclera (angle = Anatomical axis)
Recti act best in abducted position
- Obliques → Insertion : 30° to anatomical axis
Best act in adducted position
Additional action : Torsion



Eyemovements - horizontal gaze

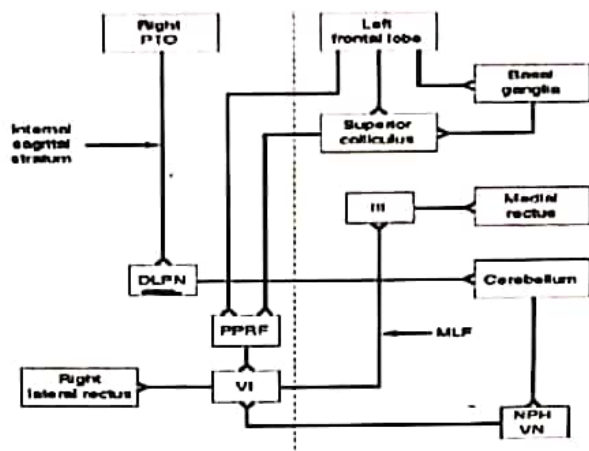
00:21:45

Horizontal Gaze

- Rapid saccades → Supra nuclear control of gaze
- arises from left frontal lobe → Frontomesencephalic pathway (FMP)
- connected to right PRRF (para pontine reticular formation)
- connected to right sixth nerve nucleus in pons
- connected to right lateral rectus

- Slow pursuit movements → peritelltemporooccipital (PTO) cortex
- ↓
- dorsolateral Pontine Nucleus

- Oculovestibular Reflex → Vestibular Nucleus → Ipsilateral 3rd Nerve
- when head is rotated - eyeball movements in the opposite direction with eye in place.



Disorders of FMP circuit

00:30:05

- Inter nuclear ophthalmoplegia : [INO]

- Upward gaze & downward gaze → Rostral interstitial nucleus in midbrain



- PTO cortex connected to Rostral interstitial nucleus

- Left MLF lesion: left III CN cannot act

↓
left MR non functional

Right LR Abduction → Nystagmus

- ie:- Same side adduction weakness, contralateral abduction nystagmus → INO

- One and a half syndrome : MLF + PPRF lesion

Eg- lesion in right PPRF + right MLF lesion → right 6th CN - Non functional
left 3rd CN - Non functional
right 3rd CN - Non functional

ie : Ipsilateral 6th CN , contralateral 3rd CN , ipsilateral 3rd CN

Not functional ; Only contralateral 6th CN Functional

↓
Abduction
(opposite eye)

Combined lesion of left MLF and PPPJ



• Ipsilateral (left) gaze palsy

• Defective left adduction

• Normal right abduction with ataxic nystagmus

Localisation :

- Frontal eye field - eyes deviate towards the site of lesion
- Thalamus - Wrong-Way eyes
- Basal ganglia / PSP - Downgaze palsy
- Pretectal area (Parinauds Syndrome) - Upgaze palsy
- Bilateral INO : multiple sclerosis
- Unilateral INO : Wernickes Encephalopathy, DM
- 8 1/2 syndrome = 1 1/2 syndrome + Unilateral Facial nerve palsy
- 15 1/2 syndrome = 1 1/2 syndrome + Bilateral Facial Nerve Palsy

Horners syndrome

00:40:02

- Sympathetic fibers involved

Horners syndrome = partial ptosis + miosis + anhidrosis + apparent enophthalmus + loss of cilio - spinal reflex

Hypothalamus

(1st order)

Neuron

↓

Neurons
spinal cord
(T₁, T₂)

2nd order

Neuron

(via thorax)

Sweating/vasomotor
fibers travel via ECA

Superior cervical ganglion

[Stellate Ganglion (c₇-c₈)]

3rd order

Neurons

Fibers following

Internal carotid A

Pupil - Course with Nasociliary

Lesion

- 1st order → Brain stem lesion
- 2nd order → Lung tumor (Pancoast)
- 3rd order → ICA aneurysm

Cocaine Test

- To confirm horner's syndrome.
- Cocaine → sympathomimetic → dilatation of pupil
- Failure of dilatation after cocaine → Horner's confirmed

Hydroxy amphetamine Test

- Amphetamine → epinephrine (sup. cervical ganglion)
- Preganglionic → pupils dilate
- Post ganglionic → No dilatation
- differentiate between pre & post ganglionic lesion

Anhidrosis (⌋) → preganglionic lesion distal to carotid bifurcation

Light reflex

00:49:09

- Pretectal nucleus & EW nucleus -----> ciliary ganglion

↓
Short Ciliary Nerves

- Lesion of optic nerve (Optic Neuritis) → Relative afferent pupillary defect

↓
marcus Gun pupil.

- Swinging flash light test : to diagnose marcus Gun pupil
- Wernicke's hemianopic pupil → distal optic tract

↓
homonymous hemianopea.



- Argyll Robertson's pupil → Light - near dissociation

↓
Light reflex - absent
accommodation Reflex - present

- Seen in Tabes dorsalis, DM, Alcoholism

- Holmes Adie pupil → due to ciliary ganglion lesion

↓
↳ young ♀ dilated circular regular pupil reacting slowly
to light and accommodation
"vermiform movements"
(loss of distal tendon reflexes)

Denervation hypersensitivity: Pilocarpine of 0.25%



Pupillary constriction

oculo motor cranial nerves

SO → 4th CN → Longest intra cranial / Sub arachnoid

Course → • Exit dorsally

• Dorsal decussation

• Thinnest CN

LR → 6th CN



• 1st affected in ↑ ICP

• Longest intradural course

CRANIAL NERVES – 2

Trigeminal nerve

00:00:19

- Cranial nerve (CN) V

- Largest CN

- mixed nerve
 - Large sensory nucleus - laterally
 - Small motor nucleus - medially

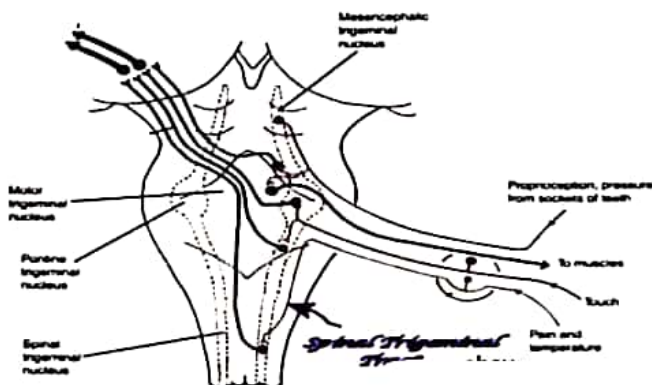
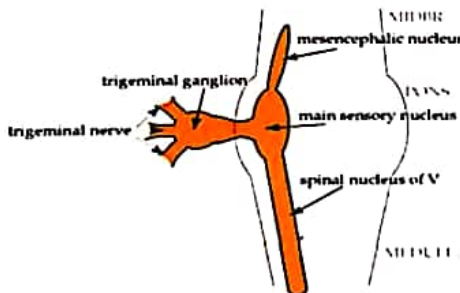
middle 1/3rd
of pons

↓
muscles of mastication, Anterior belly of digastric

- Sensory root :

has 3 parts (Nucleus) :

Gasserian Ganglion	{	• mesencephalic - midbrain → Proprioception & main centre for jaw jerk
		• main sensory - pons → Touch & temperature
		• spinal nucleus - medulla → Pain



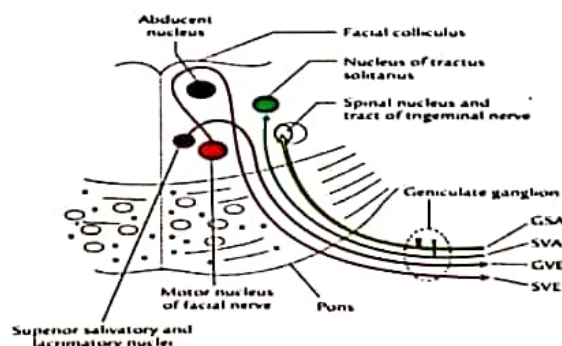
Active space

- main sensory nucleus → Cross over to opposite side
[into thalamic tract]
↓
Joins medial lemniscus
- Spinal nucleus → Descent upto c₂ level → cross over
↓
Join spinothalamic tract

Facial nerve

00:05:26

- motor nucleus [Wind around 6th CN nucleus (Facial colliculus)
muscles of facial expression, posterior belly of Digastric, Stylohyoid, Stapedius
- Sensory nucleus - Nucleus Tractus solitarius → • Taste to anterior 2/3rd of tongue
• General sensations from External ear
- Parasympathetic nucleus - Superior Salivary & Lacrimal nucleus

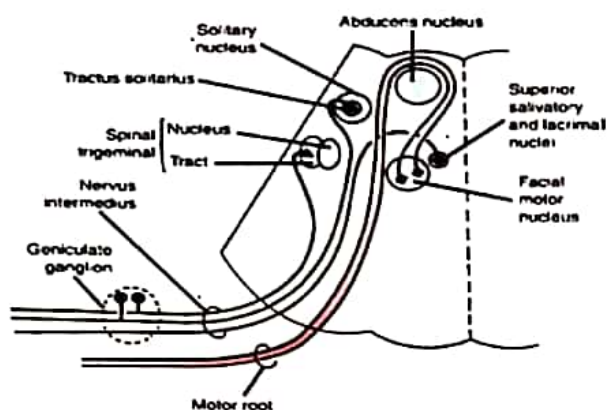


Nervus intermedius of Wrisberg → motor nucleus + Sensory nucleus

Spinal nucleus & Tract of Trigeminal nerve → General sensation

Active space

- On leaving pons :
 - motor root
 - Sensory root
 - + Parasympathetic Root
 } Nerve of Wrisberg



- Sensory nucleus :
- Nucleus Tractus solitarius → Taste to anterior 2/3 tongue
 - Spinal nucleus of V nerve

- At ponto medullary junction :
-
- motor fibers of VII CN
 - Nervus intermedius
 - VIII Nerve
 - labyrinthine artery

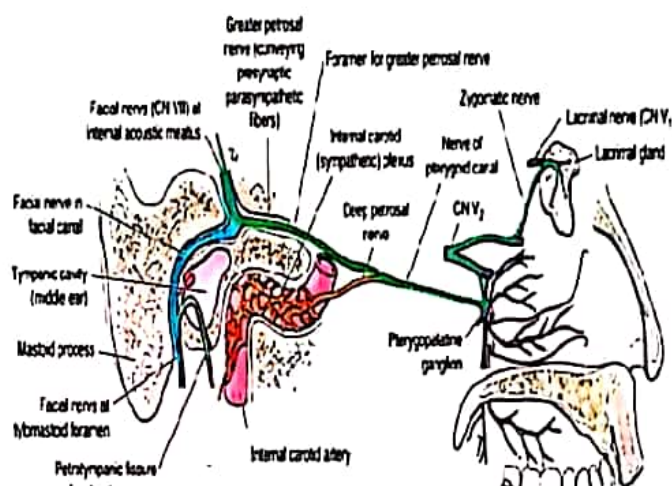
- Internal auditory meatus : Intrapetrous course
- 1st part : Internal Auditory meatus till meatus to mental foramen
- ↓
- meatal segment

- 2nd segment : labyrinthine part : narrowest part
- 3rd segment : Horizontal part : Tympanic segment
- 4th segment : mastoid part
- } Inside Facial canal (34 mm in length)

meatal foramen to geniculate ganglion - Labyrinthine part
(Inner ear)

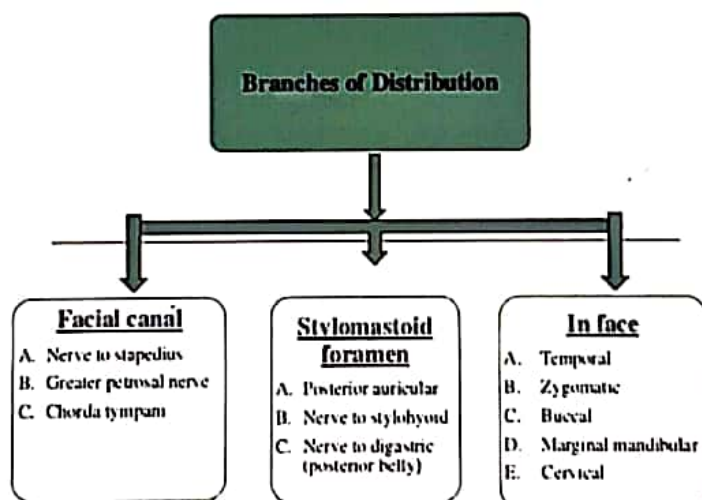
medial wall of middle ear - Horizontal part

vertical segment - mastoid part



Facial nerve : branches

00:24:03



• meatal segment → No branch

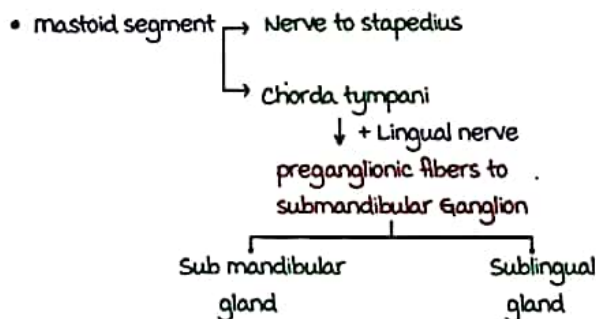
• Labyrinthine segment → At the level of geniculate ganglion

↓
Greater superficial petrosal nerve

↓ Join with deep petrosal nerve

Pterygo palatine Ganglion ← "Nerve of pterygoid canal" aka Vidian nerve

- | | | |
|---|---|--------|
| <ul style="list-style-type: none"> - Lacrimal - Nasal - Palatine | } | glands |
|---|---|--------|

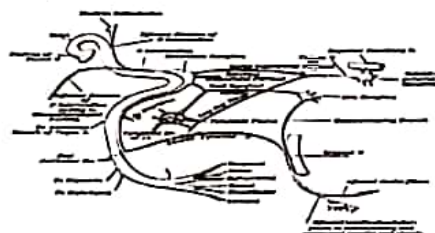


Extra cranial branches: Exits via stylomastoid foramen

- Posterior Auricular Branch
- Nerve to stylohyoid
- Nerve to posterior belly of Digastric

Inside parotid gland:

- Cervical
- Marginal mandibular
- Buccal
- Zygomatic
- Temporal



Facial nerve palsy

00:32:16

UMN



- Corticobulbar fibers seen at the level of genu of internal Capsule



Facial nerve nucleus

- Infarct (vascular ischemia) / stroke affect corticobulbar fibers

- upper part of face has bilateral representation
- Lower part of the face - unilateral representation
- UMN 7th nerve palsy → lower 1/2 of face is involved

LMN



Facial nerve nucleus



Below

- Facial nucleus
- Fibers from nucleus involvement
- Petrous Bone part involvement

- Emotional fibers → enter separately

in UMN facial palsy, involuntary emotional expression ⊕

- UMN facial palsy presentation - eg :- Right UMN hemiplegia & Right UMN 7th nerve palsy
↓ site of lesion
Left internal capsule

LMN facial nerve palsy:

- pons: Facial nerve nucleus

Unilateral LMN
Nuclear palsy

↓
Stroke

- Contralateral UMN hemiplegia
- Ipsilateral LMN 7th nerve palsy

} Crossed
hemiplegia

Bilateral LMN
Nuclear palsy

↓
At the level of brain stem:

- GBS
- Syringomyelia
- Polyneuritis cranialis (SLE, vasculitis)

- Intrapetrous part:

- Meatal
- Labyrinthine (inner ear)
- Horizontal (middle ear)
- Mastoid (mastoid process)

mcc → Bell's palsy [Idiopathic LMN]

mc Association with Bell's palsy → HSV, HZV, CMV

mc site → labyrinthine segment (Narrowest part)

LMN 7th nerve palsy → Tests for Bell's Palsy

- Forehead wrinkling (Frontalis muscle) → Absent
- Eye closure (Orbicularis oculi) → Absent

- Bell's phenomenon → On forceful closure of eye → eye moves upward → seen in LMN lesion

- Wide smile → Angle of mouth deviated to opposite side

CN → 10 & 7 → deviation to opposite side.

CN → 12 & 5 → deviation to same side.

- Whistling → ⊖
- Blowing → ⊖
- Feeding → drooling from angle of mouth on the same side, dripping of saliva
- hearing → • Hyperacusis
 - Pain behind ear
- loss of taste sensation.

Bells palsy

00:48:12

- Maximum weakness - 48 hrs
- Recovery seen in 3 weeks
- Partial palsy → very good prognosis
- Any sign of recovery within 1 week - Good prognosis

B/L LMN 7th nerve → Brain stem causes palsy

- GBS
- Syringobulbia
- Vasculitis
- SLE
- Lymphoma
- Sarcoidosis

management:

- Corneal care
- Short course steroids: Oral Prednisolone 1mg/kg/day for 2-3 weeks later taper the dose
- ± Acyclovir
- General prognosis - good

STROKE : INTRODUCTION, CLASSIFICATION AND RISK FACTORS

Introduction

00:01:24

Stroke Definition : [WHO]

- A neurological deficit of
 - Sudden onset .
 - With focal rather than global dysfunction .
 - In which after - adequate investigations, Symptoms are presumed to be of non - traumatic vascular origin .
 - Which lasts for > 24 hours .

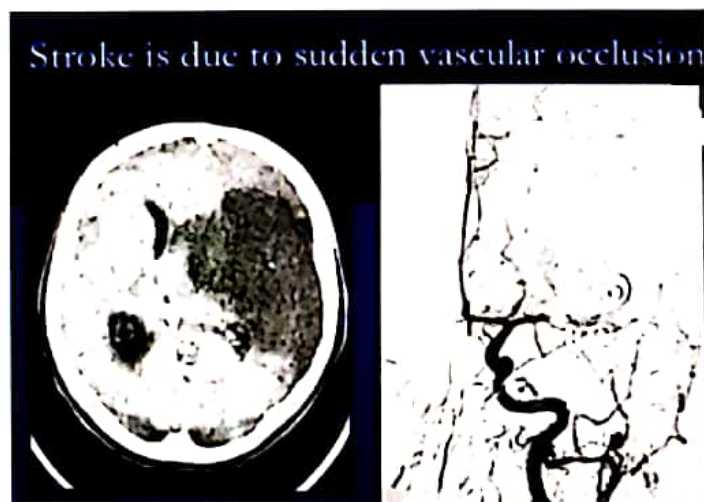
Definition Of Transient Ischemic Attack [TIA] :

- A brief episode of neurological dysfunction caused by focal brain or retinal ischaemia with clinical symptoms lasting for < 1 hr without any evidence of infarction .
- No permanent changes of brain occurs in TIA .
- Risk factor for stroke ; MI .

Investigations In Stroke

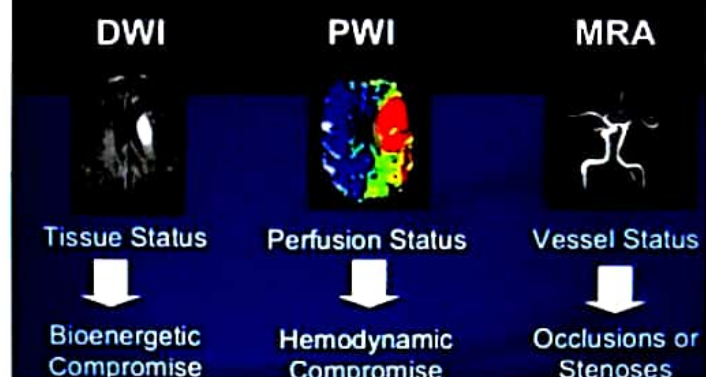
00:05:23

- CT - Angiography :

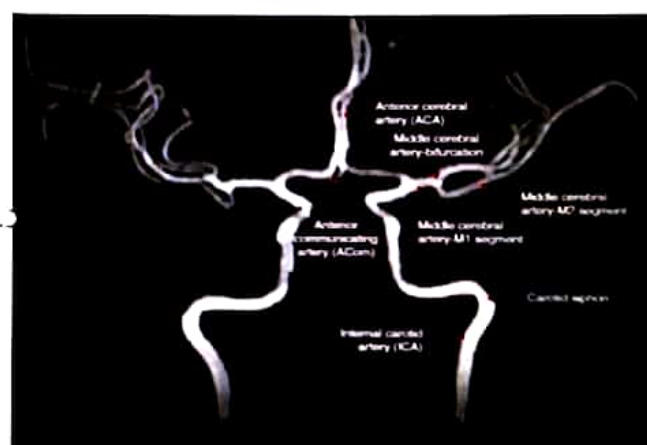


multimodal Diffusion - Perfusion MRI :

Multimodal Diffusion-Perfusion MRI



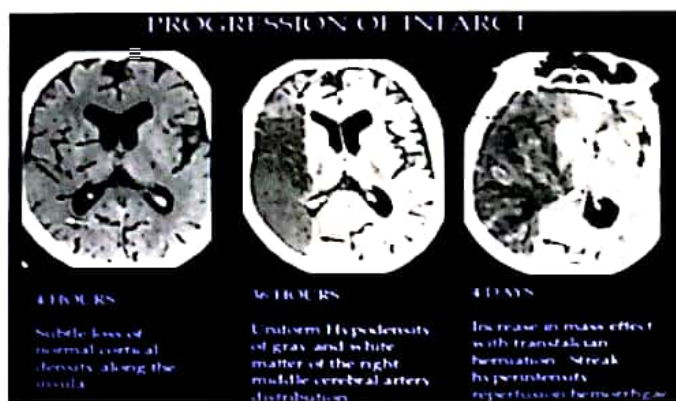
- Diffusion weighted MRI : Tissue level compromise .
- Perfusion Weighted MRI : Hemodynamic compromise – Ischemia Vs Infarction
- MR Angiogram : Site of Occlusion or Stenosis



- Diffusion weighted MRI :



- Stroke - On CT:



- CT - normal - can only exclude bleed, but not the infarct in the first 6 hours.
- Earliest CT findings in stroke - Hyperdense MCA Sign. [middle Cerebral Artery]
- Seen in 2-6 hours.



Axial unenhanced CT images in a proximal segment of the left MCA in a 53-year-old man obtained 2 hours after the onset of right hemiparesis and aphasia, show areas of hyperattenuation (arrow) suggestive of intravascular thrombi.

- Insular Ribbon Sign - Seen in > 6 hours.



Axial unenhanced CT image, obtained in a 73-year-old woman 2½ hours after the onset of left hemiparesis, shows hypoattenuation and obscuration of the posterior part of the right lentiform nucleus (white arrow) and a loss of gray matter-white matter definition in the lateral margins of the right insula (black arrows). The latter feature is known as the insular ribbon sign.

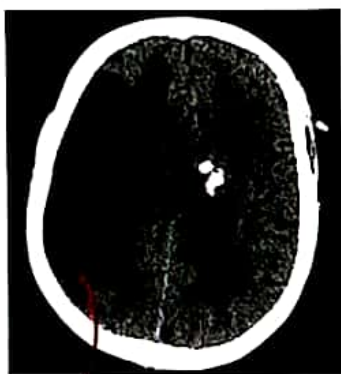
- In Insula - there is loss of Grey white differentiation .
- Obscuration and hypodensity at the level of lentiform nucleus .

Obscuration lentiform nucleus

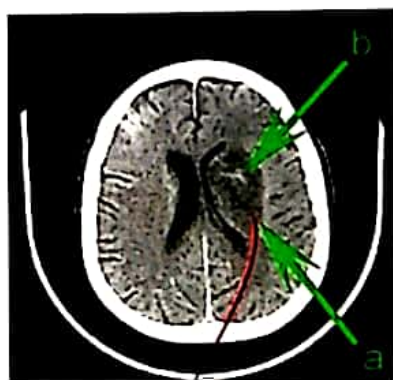
Axial unenhanced CT image shows hypo attenuation and obscuration of the left lentiform nucleus (arrows), which, because of acute ischemia in the lenticulostriate distribution, appears abnormal in comparison with the right lentiform nucleus



Subacute Infarcts



Subacute



acute

Pathophysiology of stroke

00:08:10

- Stroke is due to loss of Cerebral auto regulation .
- Cerebral blood flow = $> 25 \text{ ml / 100g} - \text{normal}$
[CBF] (50-100 ml / 100 g / min)

- $$\text{CBF} = \frac{\text{Cerebrovascular Resistance}}{\text{mean Arterial Pressure .}}$$

[MAP]
- MAP and cerebrovascular resistance adjusts themselves to maintain a constant cerebral blood flow .

- MAP from 60 - 180 mm Hg



Cerebral Blood flow remains constant (cerebral autoregulation)



In stroke : Loss of cerebral autoregulation .

- Blood flow of > 25 ml / 100 gm of brain tissue $\longrightarrow$ Normal
- Blood flow of < 10 ml / 100gm $\longrightarrow$ Infarction .
- Blood flow of $10 - 25$ ml / 100gm $\longrightarrow$ Ischemic Penumbra



Salvageable / management is done .

- Ischemic penumbra can be identified in Perfusion Weighted MRI .

Pathology of Stroke :

Loss of cerebral autoregulation



Hypoperfusion mediated $\downarrow$ in ATP



Failure of Na⁺ - K⁺ ATPase



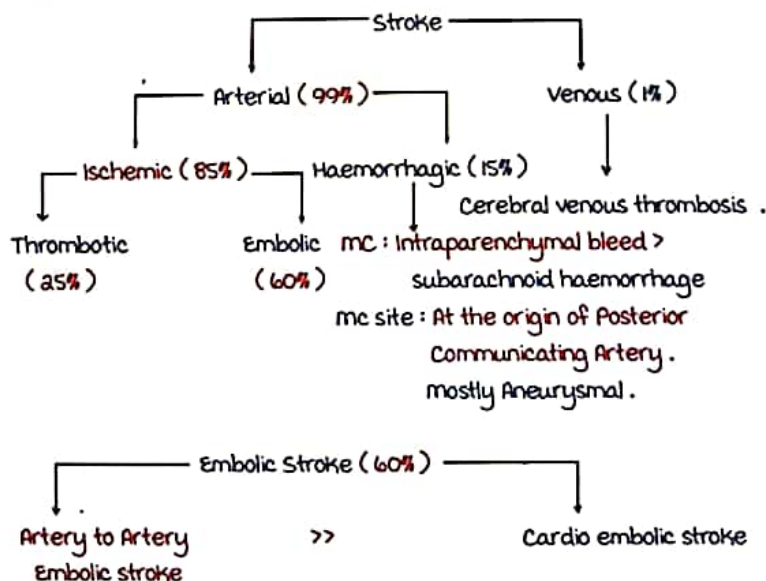
Glutamate release and Ca²⁺ entry



Liquefactive necrosis .

Classification of stroke

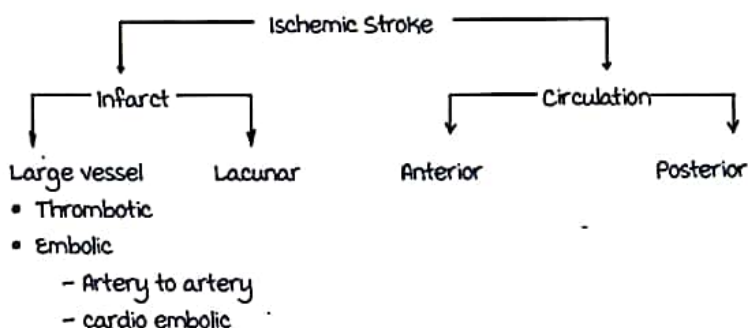
00:17:00



Lacunar Stroke :

- Seen in 30 - 300 μ m Vessel .
- Infarct Size : 3mm - 2cm
- Lipohyalinosis > Atherosclerosis .

Ischaemic Stroke



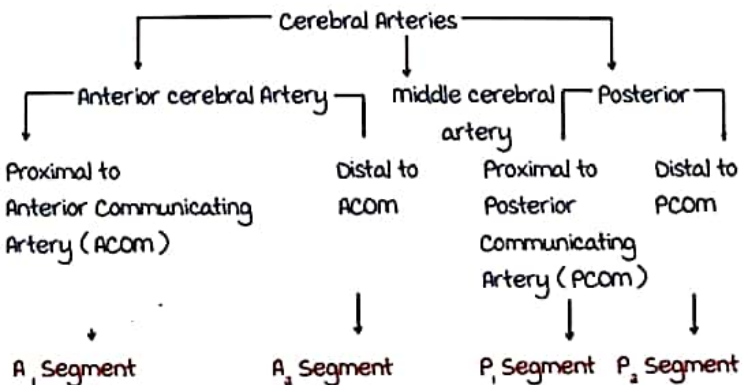
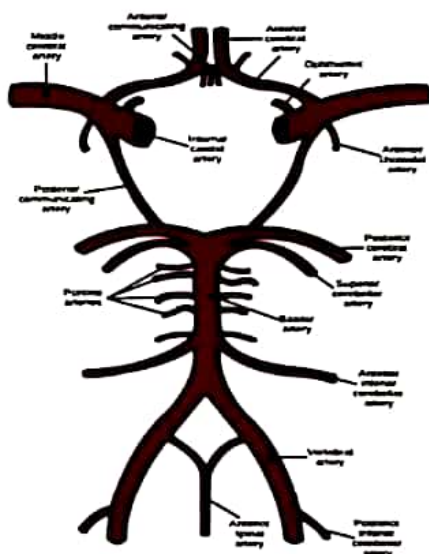
Circulation of brain

00:22:40

- Branches of vertebral artery :
- PICA (Posterior Inferior Cerebellar Artery)
- Anterior Spinal Artery

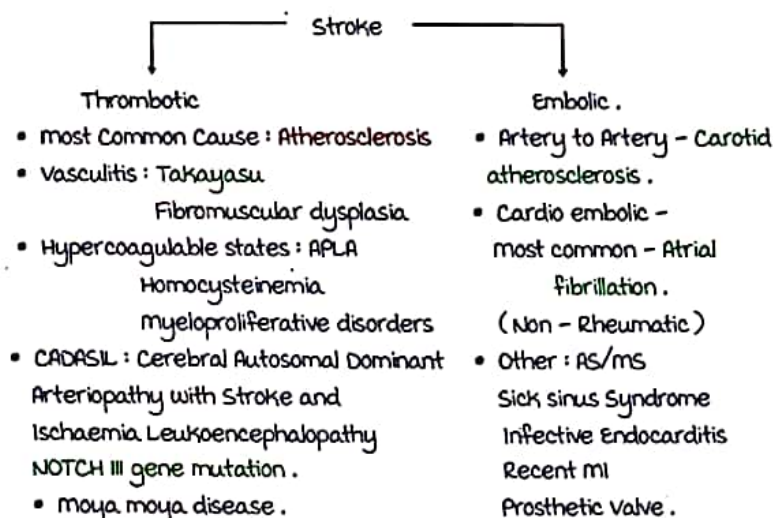
Basilar Artery

- AICA (Anterior Inferior Cerebellar Artery)
- Pontine branches
- Labyrinthine branches
- Superior Cerebellar Artery .
- Posterior Cerebral Artery



Causes Of Stroke

00:30:56



Risk Factors

TABLE 407-1 COMMON STROKE RISK FACTORS

FACTOR	POPULATION-ATTRIBUTABLE RISK	RISK REDUCTION WITH TREATMENT
LIFESTYLE		
Cigarette smoking	12-14%	50% within 1 year of quitting
Physical inactivity	30%	?
Excess alcohol consumption	7%	?
MEDICAL		
Hypertension	>90%	32%
Diabetes	5-27%	—
Atrial fibrillation	2-24%	64%
Carotid stenosis	2-7%	50%
Sickle cell disease	—	91% with transfusion therapy in children

- Non modifiable Risk factors : Age (most important), male gender
- modifiable risk factors : HTN > DM

STROKE : VASCULAR LOCALIZATION

Middle Cerebral Artery (MCA)

00:00:18

- Almost entire superiolateral Surface of Brain → MCA

- medial surface , major supply → Ant. Cerebral Artery (ACA)

- Stem of MCA
 - m_1 segment
 - m_2 segment

- m_1 segment

↓ k/a

Lenticulo striate

Branch [lacunar vessel]

↓ Supply

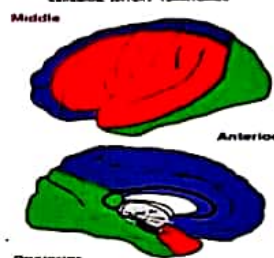
- Caudate nucleus
- Putamen
- Globus pallidus
- Posterior limb of Internal capsule

- m_2 segment

Superior division Inferior division

BRAIN BLOOD SUPPLY

CEREBRAL ARTERY TERRITORIES



Occlusion

- Stem of MCA

Effect

- C/L hemiplegia
- C/L hemisensory loss
- C/L homonymous hemianopia
- +
- Global aphasia (dominant lobe)
- Non dominant lobe involvement
 - Apraxia - constructional and dressing
 - Visual space disorientation
 - Hemispatial neglect
 - Anosognosia

Active space

- m_1 segment $\longrightarrow$ Lacunar stroke
- m_2 segment
 - Superior division $\longrightarrow$ C/L hemiplegia + Broca's aphasia + Frontal lobe features
 - Inferior division $\longrightarrow$ No weakness + Wernicke's aphasia

Lacunar stroke: Risk factor $\rightarrow$ Hypertension, elderly

- Pure motor stroke $\longrightarrow$ m_1 segment
- Pure sensory stroke $\longrightarrow$ Thalamus lesion
- Dysarthria with clumsy hand $\longrightarrow$ Genu lesion [Corticobulbar fibers]
 - $\downarrow$ m_1 segment $\downarrow$ Thalamus
 - $\downarrow$ dysarthria
- Ataxic hemiparesis

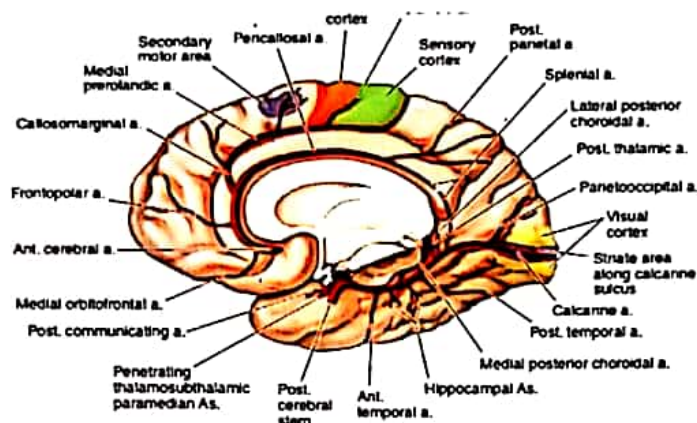
Pure motor	Contralesional hemiparesis	- Internal capsule - posterior limb - Corona radiata - Basis pontis	- Lenticulostriate branches of the MCA or - perforating arteries from basilar artery
Pure sensory	Contralesional hemisensory loss	- VPL nucleus of thalamus	- Lenticulostriate branches of MCA - Small thalamoperforators of PCA
Dysarthria-clumsy hand	Slurred speech and weakness of contralateral hand (fine motor)	- Basis pontis (between rostral 1/3rd and caudal 2/3rd)	- Basilar artery perforators
Ataxia-hemiparesis	Contralesional Hemiparesis and ataxia out of proportion to weakness	- Internal capsule - posterior limb - Basis pontis	- Lenticulostriate branches of MCA - Perforating arteries of basilar artery

Anterior Cerebellar Artery (ACA)

00:10:35

- 2 segments
 - A_1 - proximal to Anterior Communicating Artery [ACOM]
 - $\downarrow$ Occlusion
 - No clinical presentation (due to collaterals)
 - A_2 - Distal to ACOM
- A_1 supplies - Anterior hypothalamus
Anterior perforating substance
Anterior limb of Internal capsule
Anteroinferior of caudate nucleus
Amygdala (partly)

A₂ supplies :-



Lesion

A₂

effect

- C/L weakness (foot / LL weakness)
- Paracentral
- Bilateral ACA syndrome (if both branch are from a single ACA stem)



- Gait apraxia
- Primitive reflex
- Akinetic mutism

Posterior Cerebral Artery (PCA)

00:14:45

- PCA
 - P₁ - Proximal to PCOM → mid brain → mid brain syndrome
 - P₂ - Distal to PCOM → Sub thalamus, thalamus [Thalamogeniculate artery]

*PCOM = Posterior Communicating Artery

Dejerine
Roussy
Syndrome { C/L hemisensory loss with burning pain

Artery of Percheron (5-10%)

- Rare Condition (variation)
- From PCA → 1 branch → supply midbrain, thalamus, sub thalamus
- If occlusion here: Drowsiness, loss of consciousness, gaze palsies
- affects alertness / wakefulness

P₃ - supplies medial temporal lobe & occipital lobe

- On Occlusion:
 - Acute disturbance in memory
 - Visual Agnosia
 - splenium if involved → Alexia without Agraphia

Gerstman syndrome - Parietal lobe lesion → Alexia with Agraphia

Occipital lobe lesion - C/L congruous homonymous hemianopia sparing macula

if bilateral PA Occlusion → b/l Occipital lobe infarction

- ↓
- Anton syndrome
- Balint's syndrome
 - Oculomotor apraxia
 - simultaneous agnosia
 - paragnosia

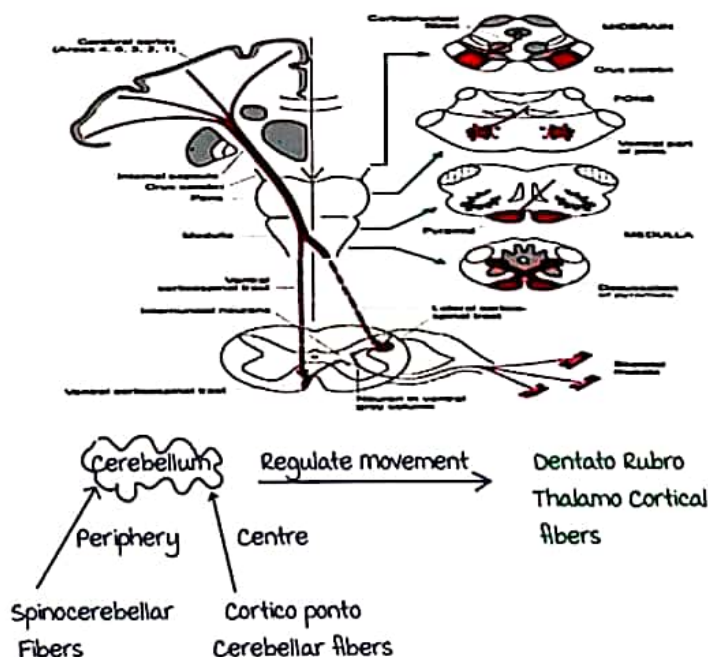
Anterior choroidal Artery

00:21:30

- Arises from Internal carotid Artery
 - Supplies lower part of posterior limb of Internal capsule
 - Occlusion → Hemiplegia
Hemisensory loss
Homonymous Hemianopia
- Ataxic hemiparesis → due to Basal Pontine Infarction

C/L Ataxia + C/L Hemiparesis

COURSE OF CORTICOSPINAL TRACT AND POSITION AT VARIOUS LEVELS OF BRAINSTEM



STROKE : BRAIN STEM SYNDROME

Brain stem- introduction

00:00:11

- ### 1) Crossed Hemiplegia :

- Corticospinal track decussates at the level of medulla.
- Lesion at level of brain stem



contralateral (UMN) weakness.

- Lesion on nuclei



Ipsilateral (LMN) cranial nerve palsy.

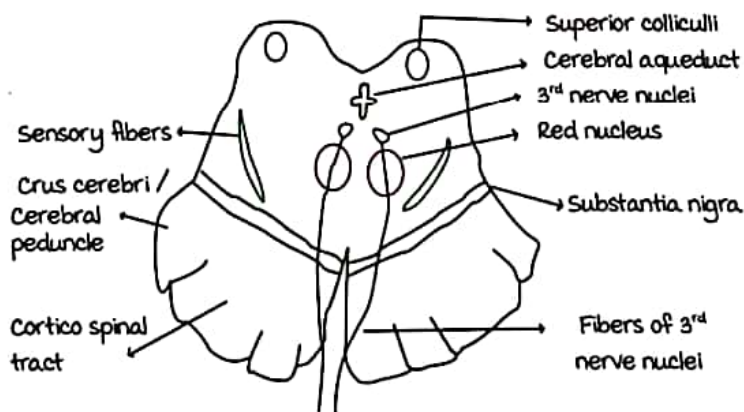
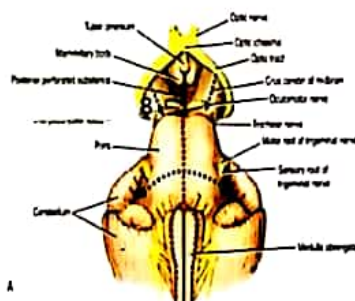
a) mid brain : Posterior view.

- Tectum:

D) Corpora quadrigemina.

a) 4th cranial nerve.

- Tegmental part :
- Forms upper parts of 4th ventricle
- median sulcus .
- median eminence (facial colliculus)
- Sulcus limitans .



Transverse section at the level of superior colliculus.

Ventral midbrain syndromes

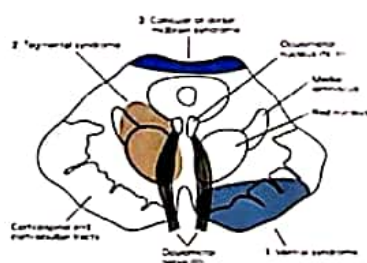
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Transverse Section at the level of the superior colliculus



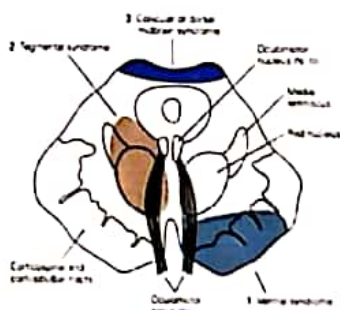
1) Weber's syndrome

- cause : Lesion at base of midbrain (crus cerebri)
- Structures involved :
 1. III nerve fascicles .
 2. Corticospinal tract .
- Deficits :
 1. Ipsilateral III nerve palsy .
 2. Contralateral hemiparesis .



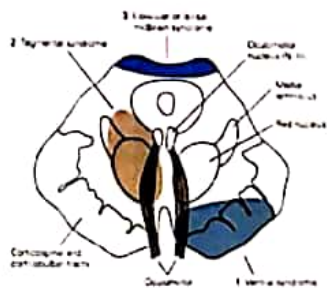
2) Claude syndrome

- cause : Lesion at tegmentum .
- Structures involved :
 1. Ipsilateral III nerve .
 2. Superior cerebellar peduncle .
 3. Red nucleus .
- Deficits :
 1. Ipsilateral III nerve palsy .
 2. Contralateral ataxia (dentatorubrothalamic tract cerebrum → red nucleus)
 3. Contralateral tremors .



3) Benedikt's syndrome

- site :
 - Tegmentum & peduncle .
 - Red nucleus .
 - Nigrostriatal pathway .
- Deficits :
 - Ipsilateral oculomotor paresis .
 - Contralateral (C/L) hemiparesis .
 - contralateral tremor & ataxia
 - C/L Hemiballismus (hemichorea, hemiathetosis)



Dorsal midbrain syndrome

00:12:17

Parinauds syndrome .

- site - midbrain dorsum .
 - Pretectal nucleus involved
 - Periaqueductal grey matter lesion
 - mc cause : pinealoma
- Deficits :
 - Impaired upgaze (pretectal nucleus is connected to rostral interstitial nucleus in the mid brain → upgaze)
 - Convergence retraction nystagmus
 - Light near dissociation .
 - Sun setting sign .
 - Colliers sign - lid retraction due to loss of supranuclear inhibitory control .
 - Skew deviation of eyes .
 - Argyll Robertson pupil → light near dissociation (accommodation reflex - present , light reflex - absent)
- Parinauds oculoglandular syndrome → associated with Tuleremia infection

Nothnagel syndrome :

- Site : lesion in the roof of tectum & quadrigeminal plate
- Features :
 - ipsilateral LMN 3rd nerve palsy
 - ipsilateral ataxia → superior cerebellar peduncle .
- Due to dorsal extension → features of parinaud's seen .

Parinaud dorsal midbrain syndrome



- Supranuclear upgaze palsy
- Normal downgaze
- Large pupils with light near dissociation
- Convergence weakness
- Lid retraction (Collier sign)
- Convergence retraction nystagmus

Pontine vascular syndromes

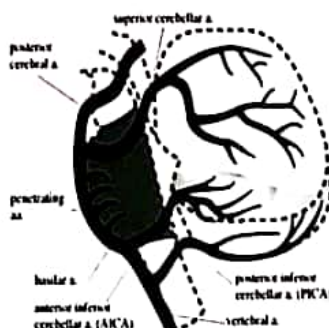
00:21:21

Vascular supply :

Anterior - Basilar artery .

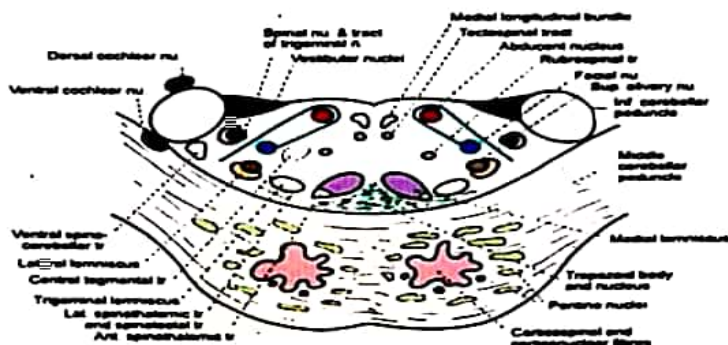
Dorsal pontine - Superior cerebellar artery .

Lateral - Basilar and anterior inferior cerebellar artery .



Active space

Transverse section through lower part of pons.



Lateral pontine syndrome :

- aka Marie - Foix syndrome .
- Blood vessel involved - anterior inferior cerebellar artery basilar artery (AICA) or basilar artery.

Involves 3 structures :

Spinothalamic tract → contralateral pain & temperature loss .

Corticospinal tract → contralateral hemiparesis .

middle cerebellar Peduncle → Ipsilateral ataxia .

Ventral pontine syndrome :

Millard-Gubler syndrome
FSH (facial nerve, sixth nerve,
contralateral hemiplegia) syndrome

- Involves basilar artery
- Contralateral hemiplegia
- 7th - 6th cranial nerve palsy .

Raymond syndrome
(SH syndrome)

- Involves basilar artery .
- Contralateral hemiplegia & 8th cranial nerve palsy .

**Dorsal pontine syndrome , Locked in syndrome ,
Top of basilar occlusion**

00:28:02

1. Dorsal pontine syndrome : Foville syndrome .

- Superior cerebellar artery involved .
- Site → dorsal pontine tegmentum in caudal 3rd of the pons .
- Structures involved →
- Ipsilateral corticospinal tract .

- Nucleus / fascicle of Fascial nerve .

- Parapontine reticular formation .

• Deficits →

1 Contralateral hemiplegia

2 Ipsilateral peripheral (LMN) facial nerve palsy.

3 Ipsilateral conjugate gaze palsy .

a) Locked in syndrome

• Site : Ventral tegmentum / pontine infarction .

• Bilateral corticospinal / corticobulbar tract involved .

• Quadriplegia .

• Consciousness (intact RAS) and vertical gaze preserved .

3) Top of basilar occlusion .

• Topmost part of basilar artery involved .

• Bilateral p2 occlusion (occipital & medial temporal lobe) + occlusion of pre-tectal nucleus

• Features :

- Ataxia .

- Amnesia .

- Altered behaviour .

- Vertical gaze palsy .

Medullary syndrome

00:34:31

Lateral medullary syndrome .

Involves :

1) Ventral artery (V₄ segment) >

Posterior inferior cerebellar artery

Structures involved :

1. cranial nerves

- nerves not involved : 1, 2, 3, 4, 6, 11, 12

- nerves involved : 5th cranial nerve

(spinal nucleus of trigeminal nerve) :

ipsilateral loss of pain & temperature

7th cranial nerve (nucleus tractus solitarius) : ipsilateral loss of taste in anterior 2/3rd of tongue.

8th cranial nerve (vestibulocerebellar fibers)

9th & 10th cranial nerve + nucleus ambiguus : dysphagia, hoarseness

Dorsal nucleus of vagus:ANS symptoms

13th cranial nerve : Horner's syndrome

2. sensory fibers

-Dorsal column : ipsilateral loss of fine touch, proprioception

-Spinothalamic tract : contralateral loss of pain & temperature.



Features : on side of lesion

1. Numbness, pain & impaired sensation on one side of face.
2. Loss of taste (anterior 2/3rd of tongue)
3. Ataxia, giddiness, vertigo
4. Dysphagia, nasal regurgitation, hoarseness of voice.
5. Horner's syndrome.
6. Nystagmus, diplopia, nausea, vomiting.

On opposite side of lesion :

- Impaired pain and thermal sensation over half of face.

Medial medullary syndrome

00:44:06

- Occlusion of vertebral artery or branch of vertebral / lower basilar

On side of lesion :

- Ipsilateral 12th nerve involvement (Hypoglossal nucleus)



Paralysis with atrophy of one half of the tongue

On opposite side of lesion :

- involves: Contralateral pyramidal tract & medial lemniscus



Paralysis of arm and leg, sparing face, impaired tactile and proprioceptive sense over one half of the body

Cruciate paralysis :

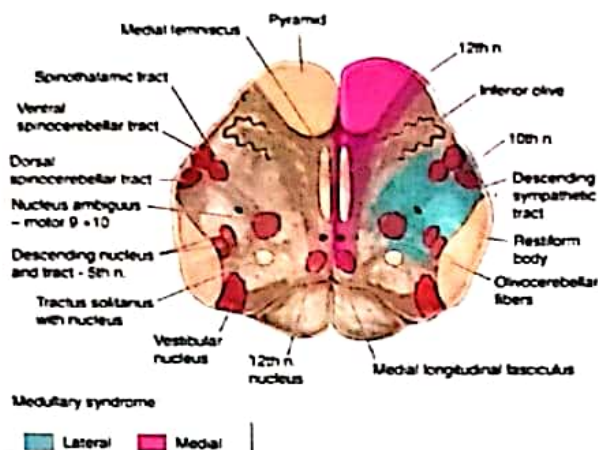
- Brachial diplegia - weakness of both arms with relative sparing of legs



due to lesion involving rostral portion of the pyramidal decussation.

or

Paralysis of one arm and opposite leg.



Avellis syndrome .

- Site : tegmentum of medulla
- Involves : (mnemonic TSH syndrome)

1 Ipsilateral tenth cranial nerve



Ipsilateral LMN 10th nerve palsy .

2 Contralateral spinothalamic tract

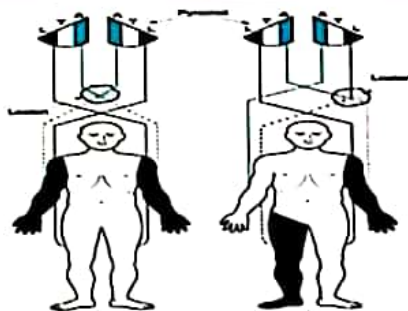


Contralateral pain & temperature loss

3 Contralateral cortico - spinal tract .



Contralateral hemiplegia



Jackson syndrome .

site : Tegmentum of medulla (Avellis + ipsilateral LMN 10th nerve involvement)

Structures involved :

- 1 Vagus nerve
- 2 Spinothalamic tract
- 3 Hypoglossal nucleus

Defecit :

- 1 Features of Avellis syndrome
- 2 Ipsilateral tongue paralysis .

MANAGEMENT OF STROKE

Stroke -Investigations

00:00:57

1) plain CT

- Done on admission
- Rule out bleeding.
- initial 6 hours → Hyperdense middle cerebral artery (MCA) sign.
- 6 - 48 hrs → Insular ribbon sign
Lentiform nuclear obstruction.
- Infarct formation requires > 48 hours.



2) T₂W MRI

- may be negative upto 2 - 4 hours post ictal period.
- MR Hyper intensity = CT Hypodensity.



Thrombolysis.

- Golden hour : within 4.5 hours.
previously → 3 hours.
- Endovascular intervention (bedside) → upto 6 hours (12-24 hours)

Indications for IV thrombolysis :

- 1) If CT brain shows no bleed, no edema, > 1/3rd of MCA.
 - 2) Patient has no pre-morbid weakness.
 - 3) No facilities for MRI.
 - 4) > 18 years age
 - 5) No history of surgery in last 21 days.
 - 6) BP < 185 / 110 mmHg
 - 7) Platelets > 1 lakh.
 - 8) No history of bleeding disorders.
- IV Thrombolysis → Alteplase (Recombinant tissue plasminogen activator)
 - Dose : Alteplase - 0.9 mg / kg.
10 % - IV stat (bolus)
90 % - infusion over 1 hour.

Note: success rate - high
rate of post lysis bleed - high

3) Diffusion weighted MRI (DW MRI)

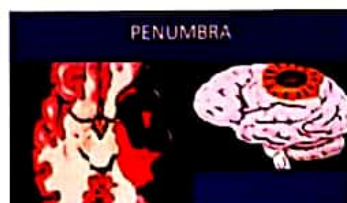
- Normal $\rightarrow$ No infarction.
- Hyperdense $\rightarrow$ infarction.



Penumbra

00:08:32

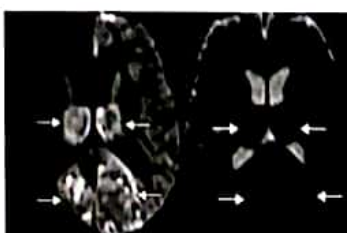
- 10 ml - 25 ml / 100g / min.
 - core of irreversibly infarcted tissue surrounded by a perihilar region of ischemia but salvageable tissue.
 - Infarct gradually expands to include penumbra.
- IOC: perfusion weighted MRI (PW-MRI)



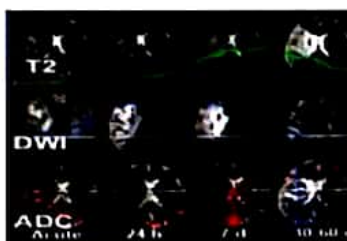
- In T2w MRI & DW MRI infarct as



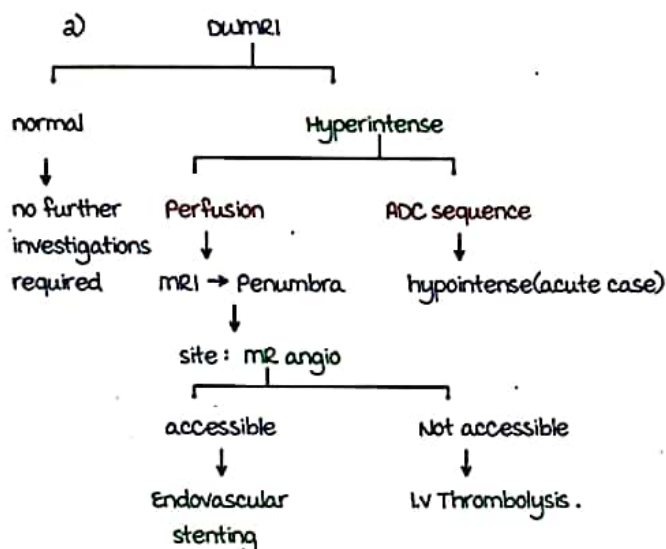
- Diffusion weighted MRI in brain infarction will be positive $\rightarrow$ for approximately 3 weeks after onset.



- ADC (Apparent diffusion coefficient) $\rightarrow$ hypointensity upto 24 hours.



1) CT brain → Rule out bleeding



NOTE :

- Aspirin : 150 mg loading dose .



In patients not eligible for thrombolysis .

- Statins → Along with aspirin for prophylaxis .
- Double anti platelet → Transient ischemic attack (TIA) , mild stroke, stroke while on ecospirin .
- Routine anticoagulants → not recommended .
- mannitol
 - 100 ml IV infusion/reason - risk of Intracranial tension is high for 3 - 5 days
- Hyperglycemia , Hyperthermia at presentation → bad prognosis .
- Carotid endarterectomy
 - done post stroke
 - unfit → carotid stenting .